

NASOPHARYNGEAL CARCINOMA

A Clinical and Pathological Study of 112 Cases  
seen in Singapore during the period  
February 1953 to April 1955.

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## PREFACE.

The material for this study was collected while the writer was Research Associate in the Department of Surgery, University of Malaya. She is glad to acknowledge her indebtedness to Professor D. E. C. Mekie for his permission to use the material in this Thesis and for his constant advice and help while this work was in progress. The author also wishes to express her gratitude to Dr J. K. Ritchie of the Radiotherapy Department, Civil General Hospital, Singapore, for providing details of radiotherapeutic technique used in the treatment of patients in this series.

Some of the cases in this series have already been quoted by the writer in four articles which she has written (two in conjunction with Professor Mekie) and which have appeared or are due to appear in the Medical Press.

SURVEY OF THE LITERATURE.

Until the end of the first decade of this century very few contributions on the subject of nasopharyngeal carcinoma were made to the literature. Of more recent years however, Otolaryngologists, Neurologists, Ophthalmologists, Radiodiagnosticians, Radiotherapists and Pathologists alike have written about this subject. In surveying the literature, therefore, one is forced for the sake of simplicity to depart from a strict historical sequence and to consider the writings on nasopharyngeal carcinoma under several broad headings. It is neither possible nor desirable to make any rigid division and the sections overlay each other in certain respects, for example the gross pathology of nasopharyngeal carcinoma has been considered with the clinical features. Many authors do not differentiate between sarcoma and carcinoma of the nasopharynx in describing the clinical aspects, and while the study of the literature has been confined as far as possible to those articles or sections of articles which deal with carcinoma this has not always been possible.



## I. Clinical Features.

The earliest report of a case of cancer of the nasopharynx was quoted by Bosworth as 1837. Fleury in 1863 described a case with invasion of the sphenoid and ethmoid bones, and softening of the adjacent brain and Sédillot in the following year described a similar invasion of the sphenoid sinus by a nasopharyngeal tumour. Verneuil and Flour (1873) mentioned a patient with vocal cord paralysis as a result of a lymph node metastasis. Shrady (1882) reported a case in which he had removed a large nasopharyngeal tumour with extensive attachments to the base of the skull, followed by brain complications and death.

Bosworth in 1889 collected reports of 5 cases of carcinoma of the nasopharynx and of 18 cases of sarcoma from the literature and added one case of each type which he had seen personally. The following year Hellat described anaesthesia of the pharynx, paralysis of the vocal cord and hemiparesis of the tongue in a case of nasopharyngeal carcinoma and Fox contributed a report of a patient with lesions of the optic and facial nerves.

Brown (1898) recorded a case where the patient lived for 4 years and 11 months after diagnosis had



been made. In the following year Heymann discussed the growth characteristics of sarcoma, carcinoma and endothelioma of the nasopharynx and the symptoms produced by each, their differential diagnosis and their surgical treatment. Nasopharyngeal carcinoma in a boy of 14 was reported by Elder in 1900.

Jackson in 1901 made a table of cases of nasopharyngeal malignancy and considered carcinoma rare as he was able to trace reports of only 13 cases in the past 20 years. Laval (1904) presented a Thesis on the subject and he was able to collect 27 instances of primary carcinoma of the nasopharynx from the literature. He discussed the clinical course, complications and differential diagnosis of the disease. Stenger in the same year reported a case of nasopharyngeal neoplasm with mastoiditis. Harmer and Glas 1907 considered that carcinoma of the nasopharynx was less frequent than sarcoma. In 1908 Baldwin described two further cases, one in a boy of 16 years.

The first important contribution to English literature was made by Trotter in 1911 when he described "certain clinically obscure malignant tumours of the nasopharyngeal wall". He had seen 13 or 14 cases, all but one of whom were male, mainly between the ages of 18 and 35. He divided the cases into

those in which the tumour projected into the nasopharynx and those in which this feature was lacking, and directs his attention to the second class where there is infiltration of the nasopharyngeal wall. Eight or nine of his cases fell into this group, all were endotheliomata and all situated in the lateral wall. Trotter pointed out the relations of the nasopharyngeal wall, namely the Eustachian cartilage, levator palati muscle, the inferior division of the fifth cranial nerve and the internal pterygoid muscle, in that order from within out. Further, he described a triad of symptoms of deafness, trigeminal neuralgia and immobility of the soft palate on the same side, caused by outward spread of the tumour from the lateral wall. The affection of the palate is not produced by paralysis but rather by infiltration of the levator palati. Closure of the jaw occurred in late cases, and enlargement of the cervical lymph nodes was a constant late feature of the disease. Digital examination of the nasopharynx normally settled the diagnosis. Trotter stressed the importance of looking for deafness or affection of the palate in all cases of trigeminal neuralgia beginning in the third division especially in young adult males. Citelli in the same year as Trotter reported five



cases of nasopharyngeal carcinoma all but one of which arose from the lateral wall. Further cases were reported in the same year, one by Brown, and one in a girl of seventeen by Guthrie, both of which suffered primarily from ophthalmologic disturbances. Aboulker (1912) described a case with evidence of compression of the nerves at the base of the skull.

Molinie (1913) emphasised cervical adenopathy as a constant early sign of malignant tumours of the nasopharynx and urged careful examination of the epipharynx where a cause for adenopathy could not be found elsewhere. In 1914 Marschik and Finzi made contributions to the literature, the latter stressing the occurrence of metastases.

Gatewood (1916) was able to trace only 26 cases of nasopharyngeal malignancy in the literature since Laval's Thesis but felt that the disease was uncommon only because it was unsuspected. 60% of cases occurred between the ages of 40 and 60 but he reported a case in a boy of 9 years. He described the methods of extension of the primary growth as (1) pharyngeal extension to the palate, (2) lateral extension to the Eustachian tube, (3) anterior nasal extension to the anterior cranial fossa and (4) posterior cranial extension.



Oppikofer in the same year gave a very extensive list of references concerning all tumours of the nasopharynx. The fifth cranial nerve was most commonly involved in its peripheral portion but the Gasserian ganglion was involved in some cases. The vestibular reactions were all normal in his patients. He reported a post mortem of a girl of 13, the youngest of his series, in which tumour was attached to the vertebral columns but had not penetrated the dura and in 1916 he reported a further autopsy of an endothelioma where the dura mater was elevated but not penetrated. A further case with neurological symptoms was reported by Stähli in 1920. Norcross (1916) described intramural malignant tumour of the nasopharyngeal wall.

In 1919 the editorial of the Chinese Medical Journal drew attention to the frequency with which nasopharyngeal carcinoma occurred among the Chinese.

It was in 1921 that New who was to be one of the principal writers responsible for furthering the knowledge and the interest of the medical profession on the subject of nasopharyngeal neoplasms published an article entitled "Relation of nasopharyngeal malignancy to other diagnosis" and in this he stressed the frequency with which a wrong diagnosis was made in

such cases. The following year he reported seventy-nine cases of malignant tumours of the nasopharynx. He drew attention to the frequency with which nasal or nasopharyngeal symptoms were absent and emphasised that symptoms due to involvement of one or more of the Eustachian tube, cranial nerves or suggesting tumour of the Gasserian ganglion or pituitary should suggest the possibility of a nasopharyngeal neoplasm even in the absence of local symptoms. New considered that examination of the nasopharynx by means of a post-nasal mirror possibly aided by cocaineisation and by drawing the palate forward with a retractor was adequate and gave a better perspective than nasopharyngoscopes. He enumerated the symptoms in his 79 cases as follows:

Symptoms referable to the eye in 21 cases

"	"	"	"	ear	"	29	"
"	"	"	"				
				nasopharynx	"	38	"
"	"			to the			
				glands of neck	"	51	"
"	"			to the			
				Gasserian ganglion	"	4	"
"				referable to the			
				jugular fossa	"	2	"
"				referable to the			
				intracranial lesions	"	11	"

He stressed the difficulty of differentiating



intracranial and extracranial symptoms. Ankylosis of the lower jaw might occur from direct extension of the tumour to the pterygoid muscles. In 1932 New, Broders and Childrey recorded how 185 operations had been performed on 194 patients with nasopharyngeal malignancy before a correct diagnosis was made.

Woltman (1922) gave the first full survey of the neurological aspects of the disease. He selected 25 cases of New's 79 with neurologic symptoms and of these 15 were squamous cell epithelioma. He found the sixth nerve to be most frequently involved and next the fifth, both sensory and motor branches. Peculiar dissociations in the sensory disturbances of the trigeminal nerve occurred. He included lesions of the nerves of the palate among vago-accessory lesions. The eighth nerve was never involved and the first nerve could not be assessed because of nasal obstruction. He considered that the cranial nerves were usually involved extra-cranially and those passing through the orbital fissures most often. IX, X and XI might be involved at the jugular foramen by spread along the skull and not only by glandular metastases. Palatal immobility might be caused by direct pressure from tumour, paralysis of levator palati or to nerve damage. The twelfth nerve was commonly involved at



the hypoglossal canal. Woltman pointed out that the bony structures round the orifice of the Eustachian tube were mainly thin and easily eroded and that there were numerous foramina and fissures through which tumour could extend. The sphenoid and ethmoid bones were usually invaded early. Crowe and Baylor (1923) emphasise that diagnosis should not be based on microscopic examination of a small fragment without considering the clinical and laboratory findings. They also warn that taking a piece of tumour for biopsy may produce distant metastases. Thomson in the same year, writing from Canton, China, emphasises the high incidence of what he calls 'cervical lymphosarcoma' among the Chinese. He collected 90 cases of which 47% had nasal obstruction. Campo in 1923 reported a case of lymphoepithelioma of the nasopharynx from Italy.

Dobson (1924) commented on the high incidence of the disease in Chinese and suggested as a causative factor the accumulated smoke from Kerosene lamps, fireplaces, tobacco and candles in poorly ventilated Chinese houses.

Further contributions on the subject of nasopharyngeal growths were made by Milligan in the same year and by Dietrich, Ferreri and Marx-Munster in 1926.

Quick and Cutler (1927) in describing transitional cell carcinoma of the nasopharynx which is characterised by early and wide dissemination of the disease, observe that the clinical picture may be dominated by the metastatic process while the primary tumour remains undetected.

Gardham (1929) describes the lesions produced by tumours of the nasopharynx due to infiltration of muscles and of the base of the skull, confirming much of what Trotter had said. He thought that the molar branches of the second division of the trigeminal nerve might be involved as they pass over the tuberosity of the maxilla. VI nerve involvement was in his view occasional and late and was probably due to interference with its vascular supply between the point where it pierces the dura mater and enters the cavernous sinus. He disagreed with Trotter that immobility of the palate was due to infiltration of the levator palati as one would expect a raised immobile palate in that case and this did not occur. Gardham's view was that the nerves of the palate were involved by direct extension.

In speaking of the lymph node metastases he found that the upper deep cervical group was involved, and most commonly those lying on the jugular vein



behind the angle of the jaw. Invasion of the retropharyngeal glands was rare. In character the glands were hard but distinct and appeared to be fixed together early in the disease by a soft fibrous mass.

Pack and LeFevre (1930) reported two cases of epithelioma of the nasopharynx in children under 4 years of age seen at the Memorial Hospital, New York.

In 1931 Ball described a case of carcinoma of the nasopharynx with a non-functioning labyrinth which he attributed to involvement of the eighth nerve at the internal auditory meatus. Further contributions to the knowledge of neurological involvement in nasopharyngeal carcinoma were made in 1932 by Bonnahon and Hansel. Hansel quoted abducens paralysis as the commonest and earliest cranial nerve lesion, seconded by trigeminal lesions. Ballenger in the following year described a case with acoustic nerve deafness in which the internal auditory canal was found to be filled with tumour at autopsy. The dura mater was eroded in many places on the floor of the middle cranial fossa. Microscopically the tumour was a transitional cell carcinoma arising from columnar epithelium. Jacod (1934) in discussing the ocular manifestations of nasopharyngeal cancer described a



petrosphenoidal syndrome where there is unilateral neuralgia of the trigeminal nerve and total unilateral ophthalmoplegia due to involvement of II, III, IV and VI.

Ruedi and Zuppinger (1934) described a method to aid diagnosis of nasopharyngeal neoplasms by injection of a radio-opaque substance into the nasopharynx, a filling defect being produced in the presence of a tumour.

Ch'eng writing from Peiping in 1935 saw seven patients in 5 years with cranial nerve lesions. All were male and chiefly middle-aged. In 6 cases no primary tumour was detected. The cranial nerves were involved 4 - 11 months after the onset of disease. He thought that the optic nerve was involved by interference with its venous return which while not severe enough to produce cavernous sinus thrombosis caused hyperemia of the discs, papillitis and disturbances of vision. The eighth nerve was never involved, Rinne's test being negative in all cases with deafness. A post mortem report of a case with gross tumour involvement at the base of the skull, describes a tumour deposit at the cerebropontine angle, with the fifth to twelfth cranial nerves embedded in tumour.

In the same year Roger and Paillas described the

multiple cranial nerve paralysis which were produced by extension to the base of the skull by rhinopharyngeal tumours; and further views on the subject were expressed by Heine.

Salinger and Pearlman (1935) list cervical adenopathy, tubal catarrh causing deafness and tinnitus and pain in the distribution of the fifth cranial nerve as the most frequent and most significant findings in malignant epipharyngeal tumours. They consider that symptoms due to cranial nerve involvement other than that of the trigeminal nerve indicate infiltration through the basal foramina orbital fissure or jugular fossa and that the disease is then hopeless in nature. They describe a proliferative group of primary nasopharyngeal tumours which are mainly sarcoma or late stages of carcinoma.

Additions to the radiodiagnostic knowledge of nasopharyngeal carcinoma were made by Kienbock and Selka and by Kraus. Keinbock and Selka (1935) in describing the skeletal metastases of Schmincke's tumour claimed that they were characteristic in producing multiple areas of destruction involving mostly the upper surface of the bone and extending into the depth - the upper surface and deep projections being connected by calcareous masses. Kraus compared



autopsy material with X-Ray films and found that the roentgen demonstration of destruction and invasion was essentially correct.

Roger et al (1936) described a case of unilateral globus paralysis of all twelve cranial nerves in a patient with epithelioma of the nasopharynx. Facial neuralgia was the first sign.

In 1937 further papers were published dealing with the neurological aspect by Needles and Schlivek. Schlivek who had previously written of Schmincke's tumour in 1932, concerned himself with the ocular manifestations of the disease which occurred in 16 of his 38 patients. Horner's syndrome was a common finding. Two patients exhibited the syndrome of the sphenoidal fissure with paralysis of III, IV, VI and of the ophthalmic division of V. Cranial nerves were all involved at the basal foramina. He found that the cervical sympathetic was involved higher up than the cervical region in many cases, and in 5 cases where no glands were palpable and concluded that Horner's syndrome was not due to lymph node metastases.

Needles found neurologic manifestations of the disease in 16 out of 35 cases of nasopharyngeal malignancy and stressed that these symptoms might appear while the primary tumour remained silent.

The average duration of the disease in the series was 28 months. He found that VI, V, III, IV were most frequently involved in that order, the lower cranial nerves less frequently, and the first two cranial nerves rarely. The auditory nerve was never involved. He mentions one case of involvement of the pyramidal tracts.

Hauser and Brownwell (1938) saw 50 cases of nasopharyngeal malignancy in 10 years, all pathologically proven. The average time of diagnosis was one year, and at that time more than 50% had enlarged glands. They mention pain in the throat as a fairly frequent symptom.

Furstenberg (1938) decided that "malignant disease of the nasopharynx presents a most provoking clinical problem and one with a prognosis as futile as that of cancer in any field within the domain of the otolaryngologist." He summarised the indications of nasopharyngeal neoplasm as (1) cervical adenopathy, (2) pain referred to ear or throat, (3) unilateral deafness or stuffy full sensation in the ear and (4) changes in the Tympanic Membrane which consist of retraction of the drum-head, and a liver coloured appearance of the drum which may cast a bluish tinge. These changes are due to negative pressure within the



typanum and are associated with circulatory disturbances in the Eustachian tube and middle ear.

Dunlap (1938) was another writer who commented upon the frequency of the disease in Chinese. In his private practice in Shanghai he saw 16 cases of nasopharyngeal carcinoma in 6 years, all in orientals. Of his patients in general only 40% were Chinese. He found early metastases to the glands of neck were rare. He quotes Green of Changsha who found 16 cases of nasopharyngeal carcinoma out of 336 tumours.

Martin (1939) found that the first lymph node involvement occurred high up behind the angle of the jaw. The adenopathy increased rapidly, often with pain and the jugular foramen syndrome was produced by pressure of glands causing nasal regurgitation of fluids, dysphagia for solids and hoarseness. There might also be involvement of the hypoglossal nerve and Horner's syndrome. He mentions the frequency of lung and mediastinal metastases after radiotherapy, and had seen metastases also in stomach, mesenteries, kidney, spleen and spine. He quotes two cases of pulmonary osteoarthropathy in carcinoma of the nasopharynx.

Weinberger and Capps in the same year reviewed the features of nasopharyngeal malignancy, and further descriptions of the disease were given in the following

year by Curry and Freidberg, Martin and Blady, and Hardy. Regarding the incidence of nasopharyngeal carcinoma Dargeon found 7 cases in children in seven years. Next to retinalglioma the most common cancer of head and neck in children occurred in the region of nasopharynx, tonsil and soft palate. Martinez reported a high incidence of nasopharyngeal carcinoma among the Chinese of Cuba. In 1941 Digby, Fook and Che gave an excellent description of nasopharyngeal carcinoma as seen among the Chinese of Hong Kong. As far back as 1930 Digby had been contributing to the literature on this subject and this paper summarised and amplified his previous work. Carcinoma of the nasopharynx was the second most common form of cancer in Hong Kong accounting for 18% of all forms of malignant disease. In making a diagnosis, 'adenoids' in children under 15 and nasopharyngeal fibroma in young people from 15 to 25 years had to be considered. They allocated a system of marks for various clinical signs by which they evaluated the validity of a diagnosis of nasopharyngeal carcinoma. The only theory of aetiology to which they attached any importance was that of Dobson. The greatest number of their 210 cases occurred between 36 - 40 in men and between 31 - 35 in women. The sex ratio of



males : females was 3.2:1. Nasal obstruction occurred as a late feature of the disease in 59% of cases and ear symptoms in 71%. They stress that the cervical glandular enlargement is nearly always asymmetrical and asynchronous which is of much diagnostic value. The first glands to be involved are the upper deep cervical beneath the anterior border of sterno-mastoid, but the posterior triangles may become involved later. A very full description with photographs is given of the cranial nerve lesions but the frequency with which different nerves are involved is not given.. Digby later (1951) discussed the aetiology more fully. Possible factors which had been suggested to be causative in the occurrence of nasopharyngeal carcinoma among the Chinese included (1) eating hot food, which Digby pointed out did not reach nasopharynx (2) hawking of phlegm, but the nasal passages of average Chinese are broader and less subject to catarrh than those of most other nationalities, (3) Dobson's theory which was the most possible, (4) the smoking of opium as suggested by Balasingham but many cases with the disease were not opium smokers and (5) an intracellular virus but one would expect the disease to be transmitted by droplets and it was extremely uncommon for members of one family to suffer from the disease.

Lymphatic spread may be by embolism or permeation, and Digby points out that if it were by embolism it would suffice to remove the primary tumour and lymph nodes separately, whereas if by permeation the whole intervening tract must be extirpated. Paralysis of the soft palate on one side with deviation of the uvula to the opposite side probably signifies failure of the accessory fibres running through the pharyngeal plexus.

Bercovitz in 1941 writing from Hainan China noted that cancer of the glands of the neck was the most frequent form of malignant disease there, i.e. 21.5% of 451 cases. Most occurred in people under 40, in men and in farmers. Many cases left no doubt as to the location of the primary in the nasopharynx, although in many the primary could not be located and it was impossible to obtain autopsies in Hainan.

Only 2 cases of Hodgkin's disease were seen. North of Canton and Hong Kong cancer of glands of the neck was uncommon, and even in Canton and Hong Kong it was less common than in Hainan.

Figi (1941) reported squamous cell carcinoma of the nasopharynx in a boy of 11 years which responded to radiotherapy. He stressed that the mortality due to carcinoma in children is extremely high, and that most cases of nasopharyngeal carcinoma terminated in



death in from 2 months to 3 years. Kasabach wrote of the disease in the same year. Jönsson (1941) used air in the nasopharynx as a contrast medium in the diagnosis of tumours of that region, a method which had previously been described by Ducuing and Ducuing (1933). The tumour appeared as a soft tissue shadow bulging into the air filled lumen. The shadow could not be definitely differentiated from that of adenoids or inflammatory conditions but it was nearly always situated asymmetrically while the other two lay in the mid-line. Carcinoma of the nasopharynx had much greater destructive tendency than did sarcoma but there was no difference in the actual appearance of the destruction. He divides the destruction into two groups, (1) the larger, localised in the posterior part of the middle cranial fossa around F.lacerum and ovale and (2) situated round the sphenoid sinus and medial pterygoid lamina. The destruction was seldom bilateral. Every case with symptoms due to involvement of the nerves to the eye muscles or of the first two divisions of V showed distinct destruction of the base of the skull.

Lenz (1942) found that there was invasion of the skull in 10 of 15 patients with a primary tumour near the Eustachian tube and in only 4 of 19 where the

primary was near the pharyngeal tonsil.

Persky (1943) reports a case of a woman of 52 who was first seen with a tumour of the tonsil and a year later a mass was found in the nasopharynx. The author considered them to be separate growths, both were lymphoepithelioma histologically.

Belanger and Dyke (1943) reviewed the radiological changes in the skull in 14 cases of carcinoma of the nasopharynx. Only two cases showed proliferation of bone and in one it was combined with destruction - all the other cases show destructive changes. Intratumoral calcification was not seen. The structures most commonly involved were, (1) body of sphenoid, (2) basiocciput and (3) medial margin of greater wing of sphenoid. The sella turcica might be eroded. They emphasise the importance of a stereoscopic basal projection of the skull but admit that clues may often be gained from examination of the lateral film. Soft tissue changes were noted in the para-nasal sinuses, in the nasopharynx and in the sphenoid sinus.

Burman and Burman, and Eggston made further contributions to the literature in the same year.

Wang writing from Chengtu, China in 1944 had seen 36 cases of nasopharyngeal malignancy, 92% of which were carcinoma, in  $6\frac{1}{2}$  years. The primary tumour



commonly arose in the lateral wall, especially from the Fossa of Rosenmüller and was usually small, irregular and non-pedunculated, ulcerated and covered by a layer of greyish white exudate. The regional lymph nodes were rubbery hard, usually bulky and lacked sharp definition, and were involved in 45% of cases. The disease ended fatally in  $2\frac{1}{2}$  years to 3 years 4 months irrespective of treatment.

Stevenson and Eckhard reported myelomalacia of the cervical portion of the spinal cord following radiotherapy for lymphoepithelioma of the nasopharynx. 6,000 - 8,000 roentgen had been given at the level of the spinal cord.

Nielsen reported 77 cases of malignant nasopharyngeal tumours in Copenhagen between 1931 - 41, which comprised less than 1% of all malignant tumours. The ages varied from 16 - 76 years, and he considered that age did not play any noticeable role in the roentgenologic prognosis. One case developed diabetes insipidus which was thought to be due to tumour invasion of the posterior lobe of the hypophysis.

Whiteleather (1943) considered transitional cell carcinoma to be the most common nasopharyngeal tumour, accounting for over two thirds of cases. He thought that cranial nerves were more often involved in the

cavernous sinus than at the basal foramina.

Martin in his chapter on nasopharyngeal tumours in Jackson and Jackson's 'Diseases of the Nose, Throat and Ear' describes the nasopharyngeal tumour as arising most commonly in the posterior wall in the region of the nasopharyngeal tonsil and its lateral extensions into the recessus pharyngis and next commonly from the ridge which surrounds the orifice of the Eustachian tube in the lateral wall. He thinks that nasopharyngeal carcinoma is much more common than reports in the literature indicate, and that it occurs at an earlier age and more often in children and in people below the age of 30 than any other malignant growth of the upper alimentary and respiratory tracts.

Flynn (1946) described a case with involvement of all twelve cranial nerves.

Ackerman and Regato (1947) give a very full description of nasopharyngeal neoplasms. They divide the primary tumours into three groups, (1) ulcerated lesions arising from the posterior and lateral wall behind the Eustachian tube, with a tendency to spread to the middle cranial fossa and there involve the second to sixth cranial nerves, which are well differentiated epidermoid carcinoma, (2) lobular which arise from the Eustachian tube area, spread laterally



and downwards, and upwards only late in the disease which are lymphoepithelioma or undifferentiated epidermoid carcinoma and (3) exophytic, arising from the roof, spreading through the choanae and to the maxillary sinus and orbit, and are usually lymphosarcoma. In speaking of the cranial nerve lesions, they describe the syndrome of the retroparotidean space where IX, X, XI, XII and the cervical sympathetic may be involved.

Davis (1947) divides the symptomatology of tumours of the nasopharynx into four groups, (1) auricular, (2) glandular, (3) neurological and (4) nasal.

Williams (1947) speaking of the frequent location of nasopharyngeal carcinoma in the Fossa of Rosenmüller pointed out that this lay directly below the Foramen Lacerum and that the tumour could therefore progress by soft tissue continuity to involve the cranial nerves extradurally.

Godtfredsen (1947) discussed the ophthalmoneurological symptoms of the disease. He was able to trace over 2,000 cases of nasopharyngeal cancer from the literature and had himself collected 454 cases from the four Scandinavian Radiological Clinics in 10 years. They constituted 0.4% of all cases of cancer. 38%

of these exhibited ophthalmo-neurological symptoms. He stressed the ability of these tumours to infiltrate the surrounding tissues particularly the parapharyngeal space and the base of the skull. Spread could occur through the Foramen Lacerum, thus to involve the nerves in the cavernous sinus either by pressure or direct invasion and then upwards and forwards to involve the optic nerve. Exophthalmos could result either from an extension of this growth through the superior orbital fissure or by spread to the inferior orbital fissure via the parapharyngeal space. The cervical sympathetic could be injured by spread through the parapharyngeal space, in the paratrigeminal area or in the cervical region. He analysed the symptoms at three different stages in the disease, (1) at an average of 11 months before diagnosis is made, (2) 4 - 5 months before diagnosis and (3) at the time of diagnosis. At the time of first analysis nearly all patients were monosymptomatic. By the second analysis the ophthalmoneurological symptoms had doubled in frequency and only a quarter of patients had only one symptom. In the third analysis ophthalmoneurological symptoms were almost the same as at the second analysis, and therefore occurred early in the disease. Glandular metastases increased steadily in frequency at each analysis.



The initial neurological symptom was trigeminal neuralgia in 71% of cases, usually in the second division of the nerve. He described a new syndrome namely ophthalmoplegia (usually of VI) combined with a lesion of XII, and sometimes associated with a trigeminal lesion. He claimed that this indicated invasion round the cavernous sinus plus a compression of the hypoglossal nerve by glandular metastases as it emerged from the anterior condylar canal and was therefore pathognomonic for cancer of the nasopharynx.

Fox (1948) enumerated the most important early symptoms of the disease as being cervical adenitis, earache or deafness - haemoptysis and nasal obstruction. Metastases occur early. Out of 12 patients 2 survived for 5 years. One patient had tumour tissue in the middle ear but it was impossible to determine whether this had spread via the Eustachian tube or from the petrosa.

Boyce and Bolker writing of the ocular manifestations of nasopharyngeal carcinoma in 1949 found that they occurred in 32% of their series, being multiple in 54% of those affected.

In the same year Baylin, Reeves and Kerman analysed the radiological changes in the skull due to nasopharyngeal neoplasms. In order of frequency

these were (a) abnormalities of nasopharyngeal airway, (b) destruction of basiocciput, (c) involvement of basal foramina, (d) abnormality of petrous tip, (e) changes in sella turcica, (f) vomer involvement and (g) optic foramen erosion, in all of which last exophthalmos occurred. They considered that while ethmoidal, sphenoidal or even nasopharyngeal soft tissue abnormalities will not establish diagnosis, if any or all are accompanied by basiocciput, petrous tip or basal foramina destruction, a diagnosis of nasopharyngeal malignancy should be reached.

Grotts described a case of transitional cell carcinoma of the nasopharynx in a 29 month-old child.

Simmons and Ariel (1949) presented a series of 150 cases. They estimated the incidence of nasopharyngeal carcinoma as 0.7% of all malignant neoplasms. The patients were all male, of average age 45 years, 88% white, 11.3% negro and one was Chinese. The tumours arose usually in the Fossa of Rosenmüller and might be bulky and fungating or soft and infiltrating. The order of frequency with which cranial nerves were involved was VI, XII, V. All twelve cranial nerves were involved in two cases, where Horner's syndrome was also present. Cervical



metastases were common and early. Generalised metastases are stated by these authors to be more common in nasopharyngeal carcinoma than in any other form of intra-oral cancer. 128 of the series were dead, their average duration of life having been 27 months, but it was noted that while the life expectancy of those who had had radiotherapy was 31 months, those who had not been treated with X-Rays lived only 17 months. There were no cures among those with bilateral cervical glands and no survivals for 5 years of those who had intracranial involvement. The 5 year survival rate was 9.8%

Mekie (1949) quoted nasopharyngeal carcinoma as the third most common form of cancer in Singapore; accounting for 87 (16.41%) of 530 cancer cases. He had never seen the disease in a patient other than Chinese or of Chinese extraction. He describes two gross nasopharyngeal tumours which have different clinical characteristics, (a) the bulky form which does not metastasise to the cervical lymph nodes till late in the disease and (b) the small ulcerative lesion which produces early and widespread lymphatic enlargement. He describes as typical of the disease "the Chinese man of middle age who sits - with his head in his hands and - looks up with an internal strabismus."

He mentions a hitherto undescribed route of tumour spread, in which the occipito-atlantoid ligament was penetrated and tumour then grew up into the cranium extradurally to involve the cranial nerves.

Hickey reviewing the literature on malignant tumours of the nasopharynx still felt that it was "an overlooked condition". Hara mentions the higher incidence of nasopharyngeal carcinoma among Southern Chinese than Northern Chinese and concluded that this spoke for a hereditary influence. Nasopharyngeal malignancy among the Japanese was also limited to those from the south part of the island. McNaught speaking of the disease in San Francisco which has the largest community of Chinese outside China said that the incidence of nasopharyngeal carcinoma there was 20 times more common among the Chinese than among the white members of the community.

Martin and Quan (1951) also discuss the high racial incidence of the disease among Chinese. They discount Dobson's theory of a smoke-laden atmosphere in poor housing conditions as the disease still occurs with unusual frequency in Chinese living in good environments, for example those living in America. They conclude, therefore, that the tendency is racial. In the Memorial Hospital, New York, 71% of cases of



cancer of the upper respiratory and alimentary tracts among orientals had the primary in the nasopharynx, whereas the same figure for the all-over population was 5.5%. All the orientals with carcinoma of the nasopharynx in this series were Chinese.

Jefferson (1953) found that symptoms of invasion of the cavernous sinus and the trigeminal nerve were the first sign of nasopharyngeal malignancy in one third of cases. The cavernous sinus was invaded by tumour extension through Foramen Lacerum, thence to Gasserian ganglion and thus to the sinus. He considers that unilateral palsies of several nerves or inconsequent palsies perhaps with Horner's syndrome are suspicious of nasopharyngeal tumours. Many neoplasms described in the literature as endotheliomas of the trigeminal sheath were probably really primary in the nasopharynx.

In 1954 Battory reported a case of lympho-epithelioma in a girl of 10 years. Mekie and Lawley made a clinical analysis of the features encountered in 120 cases of nasopharyngeal carcinoma seen in Singapore from 1947 - 1954, some of which are included in this Thesis. Das et al reported nasopharyngeal cancer as constituting 1.85% of all cancer cases seen in the Punjab. 81% of their cases were male and the

ages varied from 7 to 70 years.

Lambert (1954) quoted the incidence of carcinoma of the nasopharynx as 6 in one million for the north west region of England. After adenopathy, nasal symptoms were the most common warning of nasopharyngeal malignancy.

Flatman considers that the number of combinations of cranial nerves affected is so wide that it is inaccurate to regard any one as a syndrome, but that the combination of nerves affected may give some indication of the extent and site of spread. He points out that the nerve of the pterygoid canal, the maxillary nerve and the abducens nerve lie in a direct line above the Fossa of Rosenmüller and that disturbances of lachrymation due to injury of the nerve of the pterygoid canal should be an early sign of disease.

Lederman (1954) found that the cranial nerves might be involved via the cerebral spinal axis without obvious invasion of the base of the skull. Tumour enters the subarachnoid space via the nerve sheaths or perineural lymphates.



## II. Treatment.

Trotter (1911) advocated osteoplastic resection of the upper jaw in "endothelioma" of the nasopharynx but had not secured freedom from recurrence for longer than fifteen months in any of the six cases on whom he operated. Coley (1915) treated an inoperable recurrent growth of the nasopharynx which had extended into the sphenoid and ethmoid bones, producing exophthalmos and a bulging of the frontal regions with mixed toxins. The growth disappeared but recurred as soon as the dosage of toxins was reduced by half. Following a dose double the original given the growth disappeared again.

Patterson (1917) reported immediate good results following the use of diathermy in the treatment of nasopharyngeal malignancy.

New (1925) stresses the importance of histological grade with regard to treatment. Surgery offered little in his opinion. Cautery or diathermy was useful only in cases of low grade malignancy. Radium was used for more malignant cases both locally to the nasopharynx and to the neck. In epitheliomas average life after treatment was 25 months and he had one five year survival out of 21 patients.

In 1932 New, Broders and Childrey advocated that

in nasopharyngeal carcinoma, radium applied to the surface of the neoplasm should be the only treatment to the primary growth, with partial or complete block dissection of the glands of neck, preceded and followed by irradiation if the lesion was epithelioma graded 3 (Broder). In epithelioma graded 4, radium alone should be applied to the neck. They considered that the poor results obtained in the past were due to poor selection of cases. They treated only 38 out of 154 patients with nasopharyngeal carcinoma. New and Stevenson (1943) reported the end results of treatment. In all they had treated 271 patients of which 184 were squamous epithelioma graded 3 or 4. The average age was 43.3 years and ages ranged from 4 - 80. The symptomatic relief was striking, pain in the distribution of V and diplopia due to lesions of VI disappearing and the lymph nodes being greatly reduced in size. Regeneration of the bone of the posterior clinoids occurred in some cases. 8.9% of patients with squamous epitheliomata were alive after 5 years but of those who had no palpable lymph nodes when treated 15.6% survived for five years or longer. Females had a better survival rate than males.

Berven (1926) reported 5 years freedom from



symptoms in 5 of 33 cases of nasopharyngeal carcinoma treated by a combination of external irradiation with teluradium and local radium to the nasopharynx.

Pagani (1937) quoted a 20% 5 year survival rate in 26 tumours of the epipharynx with metastatic glands. The method of treatment was fractionated roentgen therapy. Small local residual tumours could be removed with an endotherm knife or treated by radium implant. Any residual lymph glands were removed surgically provided the primary growth had been eradicated.

Blady (1938) described a new instrument for the application of radium or radon seeds to tumours of the nasopharynx. Hitherto difficulty had been encountered in reaching the apex of the vault of the nasopharynx, in maintaining the instrument in its proper position during the period of irradiation and in avoiding trauma. Blady's applicator consisted of a capsule containing the radiation source, attached to a flexible steel shaft and fitted with an immobilizing attachment. Gold radon seeds were used by Blady, a total of 15 milliecuries being left in situ for 4 days, giving a dose of 1,026 milliecurie hours. The dose was repeated in 5 - 7 days if the mucositis was not severe. Martin (1939) insisted on vigorous irradiation. The

areas irradiated should extend from the lateral wall of the orbit and include the base of the skull, submental area and the upper portions of the triangles of neck. 3,000 r should be given to each side. When the reaction from this initial treatment has subsided 3,000 r should be given over the occipital region and occasionally treatment should also be given through the cheek. At the same time he advocated giving 2,400 r to the front and back of upper mediastinum - to prevent the occurrence of lung and mediastinal metastases. The entire course took 8 - 10 weeks.

Davis and Martin (1940) regarded the prognosis as 'not too unfavourable' while growth is local but as very poor if there were signs of intracranial spread in the absence of a nasopharyngeal lesion.

Lenz (1942) treated 47 cases of carcinoma of the nasopharynx between 1926 and 1938 with radiotherapy. He used two lateral fields and 2 paranasal-anterior antral fields, giving a total dose of 3,000 - 3,500 r in 6 - 7 weeks. He also gave intrapharyngeal treatment with X-Rays or radium but found wholly external treatment gave as good results as external irradiation plus intracavity radium. The prognosis was worse for those with a primary tumour near the Eustachian tube than for those with the primary in the



vault. Involvement of the cranial nerves did not necessarily mean that treatment would fail. Six patients with lymphoepithelioma and two with epithelioma were alive more than five years after treatment.

Baclesse and Dulac quoted 15% 5 year survivals from 102 cases (1943). Martin (1945) advocated treatment of the primary growth by a combination of external irradiation through the cheeks and intracavitary radiation by radium or radon, contained by a Blady applicator. Externally the growth was given 3,500 - 4,000 roentgens and the dosage from the intracavitary radium was 400 - 500 milliecurie hours. The neck should be treated also by a combination of external irradiation and implantation of radon seeds, but the extent treated should be limited to the area where there was demonstrable involvement by cancer. He considers palliative treatment of widely disseminated metastases is worthwhile, although he does not apply this to pulmonary deposits. The 5 year cure rate for patients without metastases at the time of admission was 50% and 25% for all cases.

Tice on the other hand in the same year gave 1,300 - 1,800 mgm. hours to the nasopharyngeal tumour if such were present, and gave the cervical lymph

nodes 'all the radiation that normal tissue will tolerate.'

Davis (1947) reported all his 19 cases of nasopharyngeal carcinoma treated by deep X-Ray therapy as being dead within 18 months.

Graham and Meyer (1948) out of 29 patients with nasopharyngeal malignancy reported two ten year survivals plus one patient who had lived for twelve years after treatment but then had a recurrence. Seventeen patients were dead and the average survival was 23 months. St Clair Thomson and Negus had patients in the Mayo Clinic who had lived for ten and seventeen years after radiotherapy. Martin (1949) who quoted nasopharyngeal cancer as constituting 0.2% of all malignant growths, had a 17% 5 year survival rate in patients treated by irradiation.

Cade considers that while in lymphosarcoma and lymphoepithelioma external radiation is the method of choice, 6,000 r being given to the nasopharyngeal tumour or mucosa, in squamous cell carcinoma this should be combined with intracavitary radiation - to give the same total dose.

Mekie and Ransome (1950) suggest prefrontal neucotomy as a palliative measure in cases where there is headache of such severity that it cannot be

alleviated by any drug. They treated 4 cases in this way, three of which were relieved of their pain.

Eberhard and Leaming (1950) thought one could expect a 40% five year survival rate in cases with no bone involvement treated with X-Rays. They preferred to use two small fields, one to the nasopharynx, and one to the cervical glands rather than one large lateral field because of the intense skin reaction which the latter evoked. Radium could be applied locally to the nasopharynx if sufficient radiation could not be applied externally because of skin reaction or high radiosensitivity of the tumour. They outline the general medical care which these patients require during radiotherapy, in particular emphasising the need to impress upon the patient and his relatives before treatment begins that dehydration weakness and mental depression will ensue.. They gave all patients vitamin B complex, and were forced to admit some to hospital for tube-feeding.

Kramer varies his method of treatment according to the histology of the primary growth. Where this is radiosensitive, i.e. undifferentiated with glandular metastases, he treats from the base of the skull to the clavicle en bloc, giving 3,000 - 3,500 r in 4 - 5 weeks. A further dose in small fields may be given later to



the nasopharynx or glands. Where the tumour is highly differentiated and there is no lymph node involvement, 5,500 - 6,000 r are given to the nasopharynx in 6 - 7 weeks. If glands are present, large fields are used for 2 - 3 weeks to give a total of 2,000 r, followed by small fields to primary and glands giving a total of 5,500 r in 6 - 7 weeks. His results showed an over-all 5 year survival rate of 25.8%. There was a high percentage of deaths in the first two years, and then the death rate lessens, patients who live more than four years having a good chance of survival. Lymphoepithelioma and undifferentiated carcinoma gave the best results, differentiated carcinoma responded badly and transitional cell carcinoma gave the poorest results. The high rate of local recurrence and of cranial invasion in transitional cell carcinoma is emphasised.

Schoolman (1951) calculated the recurrence rate after radiotherapy as 50%, 37% occurring within the first year.

Digby (1951) considers that if patients came early to hospital, they could be cured by radiotherapy. In his experience a few have "dragged on" for 5 years. He feels that some form of chemotherapy may eventually solve the problem. It was in the same year that Stock

in Hong Kong published an article describing the treatment of nasopharyngeal carcinoma with urethane. Of 23 patients treated, improvement was observed in 9. Stock concluded that as the disease did not normally regress spontaneously, this form of therapy was worth following up and suggested that it would be most useful if combined with radiotherapy.

Morrison (1951) advocated the use of radioactive cobalt in treating the primary nasopharyngeal tumour.

Wilson (1954) explained very fully the best methods of treatment available and indicated for malignant tumours of the nasopharynx at the present time. He stresses the necessity of an accurate clinical and histological assessment before the course of treatment is decided. Where glandular metastases are present it is essential to use external irradiation over a wide area covering the whole side of the neck down to the clavicle. In many cases it is necessary to supplement this by more direct methods, such as intra-oral X-Rays directed through the palate, the use of radium needles or of radioactive cobalt in some form of applicator inserted into the nasopharynx. Lymphoepithelioma are very radiosensitive, squamous carcinomata less so, although some of the undifferentiated types may approach the lymphoepithelioma in

their sensitivity, and the dosage and period of irradiation will have to be varied according to the sensitivity of a tumour. The use of surgery is limited to (1) securing a biopsy for diagnosis, (2) excising any residual mass of a primary growth after full irradiation has been given and (3) facilitating the application of radium needles or cobalt to the primary growth and enabling easy inspection of this after treatment has finished. Wilson had previously (1951) described a transverse palatal approach to the nasopharynx which could be used in all these cases. Cobalt however has recently been introduced to the nasopharynx in a mould attached to a palatal obturator, and to do this the transverse palatal incision is joined by a median one passing forwards from its centre. A triangle from the posterior part of the hard palate is removed and also the posterior border of the nasal septum, and more room is thus obtained for the insertion of the cobalt. When treatment is completed the fenestrum which has been formed is left open and covered with an obturator attached to a dental plate. This fenestrum is of great value for follow-up inspection or further treatment of the nasopharynx. The results of treatment with radioactive cobalt could not yet be assessed as it is still in its early stages.



Lawley and Mekie (1955) reported 30 cases of nasopharyngeal carcinoma which had been treated with urethane. Twelve of those improved after treatment but the abatement of the disease was never maintained for longer than four months. Histologically the tumours appeared more differentiated after urethane than before.

In the discussion on treatment of carcinoma of the nasopharynx held by the laryngology section of the Royal Society of Medicine (1954) Lambert gives an overall survival rate for nasopharyngeal tumours as 30% but stipulates that this figure gives no idea of the morbidity which accompanies treatment. Snelling reported 76 cases of carcinoma of the nasopharynx which had been treated in the Middlesex Hospital between 1934 and 1953. Seven of these survived 5 years. Where there was no glandular involvement and the growth was of low malignancy 5,000 - 6,000 r was given through small fields localised to the nasopharynx in 4 - 6 weeks. Where there was glandular involvement or the growth was highly malignant the neck was treated en bloc from base of skull to clavicle, receiving 2,500 - 3,500 roentgens. Recently treatment had been intensified and the results had improved. Where recurrences in

nasopharynx occurred even if accompanied by cranial involvement, repeated localised treatments to the nasopharynx were given with symptomatic relief but not in Miss Snelling's opinion with eradication of the disease. Recently the fenestration operation had been used and radium or radioactive cobalt introduced into the nasopharynx in a special applicator.

Four anaplastic carcinoma, 1 differentiated Ca., 1 lymphoepithelioma had survived 5 years. No transitional cell carcinoma had a 5 year survival. While lymphoepithelioma and the most malignant anaplastic carcinomas were extremely radiosensitive they metastasised early and might have spread beyond the area treated before treatment was complete. The differentiated tumours did not metastasise till late but were radioresistant. The best results were therefore obtained with intermediate tumours.

Wilson mentioned that investigation of the base of the skull had lately been carried out through a fenestration after treatment had been completed if nerve palsies recurred. There was often marked involvement of the base when the nasopharynx appeared healthy.

### III. Pathology.

In 1886 Retterer recognised the existence in various parts of the human body of epithelial and lymphoid elements in close relation to each other. Stöhr in 1890 discussed the same tissue. Jolly (1911, 1915) and Molier (1913) described the lympho-epithelial organs of the body where epithelium and lymphocytes were intimately related. These organs were situated in the nasopharynx, pharynx, tonsil, thymus, base of tongue and Peyer's patches of the intestine. They claimed that the stratified epithelium overlying the lymphoid tissue of these parts had a special physiological or symbiotic relationship to the lymphocytes and that the two elements formed together a structure which they named "lymphoepithelium". Jurisch in 1912 also discussed lymphoepithelial tissue.

Trotter (1911) considered the vast majority of nasopharyngeal tumours to be endotheliomata. Citelli in the same year reported 10 cases of primary nasopharyngeal tumours, 5 of which were carcinoma and of which 3 arose from the covering epithelium of the mucosa and two from carcinomatous degeneration of the epithelium of mucous glands. Kelsey and Brown (1913) found great difficulty in summarising the subject of



nasopharyngeal neoplasms as they found that tumours were not classified alike by surgeons and pathologists and that carcinoma was frequently confused with sarcoma and endothelioma.

Gatewood (1916) traced all available reports and found that 30% of all cases of nasopharyngeal malignancy were carcinoma, 60% sarcoma and 10% endothelioma. New's 79 cases in 1922 comprised 34 epitheliomas, 33 lymphosarcomas and 12 cases in which the malignant type was not determined on pathological diagnosis not made. In 1932 New, Broders and Childrey found highly malignant epithelioma to be seven times more common than lymphosarcoma. Where lymphocytes were admixed with epithelial cells they did not feel that the lymphocytes were a growing part of the tumour but that they occurred only because such cells were normally abundant in the mucous membrane of the pharynx and nasopharynx.

In 1921 Regaud and Schmincke separately described a group of highly anaplastic radiosensitive carcinomata arising from the lymphoepithelial organs of Jolly and Mollier. The main feature of these tumours was that epithelial cells and lymphocytes were intimately admixed and it was claimed that they comprised a special class of tumour which deserved the name

'lymphoepithelioma'.

Both writers describe the epithelial cells as having poorly stained, ill-defined cytoplasm, large vesicular nuclei and one or more dark staining nucleoli. Regand however described these cells as occurring in cords or columns and often forming a syncytium with the lymphocytes lying between the columns of tumour cells. Occasionally the cords might appear broken-up and lymphocytes occur between individual cells. Schmincke's description was of anaplastic epithelial cells forming a somewhat alveolar pattern, separated one from another by lymphocytes and giving a somewhat sarcomatous appearance. Derigs (1923) presented a post mortem report of a case in which she described lymphocytes admixed with the epithelial cells in the bone, lung and liver metastases. Jovin (1926) discussed the subject of lymphoepithelioma and using Derig's case as evidence claimed that the epithelial cells exerted a chemiotaxic effect upon the lymphocytes and that this accounted for the presence of the latter in metastases.

Quick and Cutler (1927) described a group of intra-oral tumours which they termed transitional cell epidermoid carcinoma. Their attention had first been drawn to this group in irradiating the cervical lymph



node metastases when they found that a certain number responded markedly to radiotherapy. On histological examination of lymph nodes and primary tumours of this group they were found to be highly cellular tumours, consisting of small uniform epithelial cells with large hyperchromatic nuclei and scanty cytoplasm occurring either in solid groups or anastomosing columns. The primary tumours were mainly of tonsil, base of tongue and nasopharynx, and their source of origin was thought to be either the transitional cells of the Schneiderian membrane or squamous epithelium which had lost its differentiated character. The constant absence of adult squamous characters was particularly noted, and the authors pointed out that squamous cell carcinoma of the oral cavity metastasised infrequently whereas these tumours spread widely and often early. They accounted for this partly by the anaplasia of the cells and partly because the origin of these tumours from deep structures, both properties which increased the frequency of metastases.

New and Kirch (1928) expressed the opinion that both lymphoepithelioma and transitional cell carcinoma were really squamous cell carcinoma graded 4. A year later Cutler divided radiosensitive intra-oral tumours into lymphoepithelioma and transitional cell carcinoma,



which latter he thought the more common of the two and which he considered to be an anaplastic squamous cell carcinoma. He admitted the frequent difficulty in distinguishing lymphoepithelioma, transitional cell carcinoma and lymphosarcoma and had found it necessary to consider the clinical findings before reaching a histological diagnosis in many cases.

Ewing (1929) reviewed the subject of lympho-epithelioma which he considered to be a particular form of epidermoid carcinoma arising from modified epithelium overlying lymphoid structures. He thought that it was closely allied to transitional cell carcinoma, arising from cells lining the Schneiderian membrane, pharyngeal crypts and sinuses and the ducts of mucous glands in the pharyngeal wall. He mentioned that quite different structures may occur in different parts of one tumour and that therefore the particular cell form of a tumour may not give a definite indication of its origin. He found that the metastases were sometimes more and sometimes less differentiated than the primary growth. He suggested that in lymphoepithelioma the admixture of lymphocytes might be due to a low grade inflammatory process but admitted that this would not account for their presence in metastases.

Gardham (1929) upheld Trotter's view that

nasopharyngeal neoplasms were mainly endotheliomata and were not epithelial in origin because of their tendency to spread widely beneath the mucous membrane without ulceration.

Beck and Guttman (1932) thought that transitional cell carcinoma probably resulted from anaplasia or metaplasia of ordinary squamous epithelium. In the same year Hoffman after studying three cases of nasopharyngeal carcinoma in the literature concluded that they were of branchiogenic origin, arising from islets of germinal tissue which begin to grow due to unknown causes, after lying dormant for years.

Christianson and McArthur (1933) were unable to trace any report in the literature of a fully differentiated squamous cell carcinoma of the nasopharynx. The cells of the tumours they examined resembled poorly differentiated squamous epithelium and in one they noticed a striking resemblance to the cells of the basal layer of squamous epithelium lining the nasopharynx.

In 1935 Salinger and Pearlman reviewed the literature and noted the widely different terminology used by pathologists in classifying nasopharyngeal tumours. They fell mainly into three groups, carcinoma, sarcoma and endothelioma but there was a



wide discrepancy in the relative proportions of each type as reported by different authors. Their view was that if epidermoid carcinoma undifferentiated squamous cell carcinoma, transitional cell carcinoma and anaplastic carcinoma were grouped together, most of the malignant tumours of the epipharynx would fall into this group. Regarding most of the sarcomas and endotheliomas reported they thought that they were really lymphoepithelioma or transitional cell carcinoma. Harvey, Dawson and Innes (1937) in their series "Debatable tumours" did not think it justifiable to regard lymphoepithelioma as a special tumour. They pointed out that non-lymphoid tissues frequently showed lymphoid aggregations about invading tumour and cited as examples seminoma and pinealoma. As lympho-epithelioma arose from mucosa or submucosa rich in lymphocytic aggregations, and often from relatively undifferentiated epithelium they thought it natural that the tumours should present a similar appearance to their site of origin. They classified lympho-epithelioma as either epidermoid carcinoma i.e. the transitional cell carcinoma of Ewing, or lymphosarcoma. Bonne (1937) in his paper "Cancer and Human Races" speaks of the high incidence of malignant tumours of the lymph nodes of the neck in the tropical countries of the





Far East. He describes a tumour closely resembling that called lymphoepithelioma by other authors, and designates it Reticulo-endothelioma. Although admitting the resemblance to lymphoepithelioma and transitional cell carcinoma he did not think that the 'reticuloendotheliomata' were secondary to primary nasopharyngeal tumours or that when a tumour was present in the nasopharynx this was necessarily the primary growth.

Munro Black (1938) in discussing the lympho-epitheliomata pointed out that if the lymphocytes took an active part in tumour formation either one must accept the entity of lymphoepithelium or regard the tumours as lymphosarcoma. In the same year, Cappell gave an excellent account of lymphoepithelioma. He described and illustrated by photomicrographs the original tumours described by Regaud and Schmincke and added to these a third group of transitional cell carcinoma. This differed from the first two in having a more definite origin from surface epithelium and in the absence of lymphocytes. He thought that the Regaud and Schmincke types of lymphoepithelioma merged one into the other and could not be sharply demarcated. He did not include tumours with Keratinisation or wide prickle cell formation in the third group. He

definitely accepted lymphoepithelioma as a pathological entity and thought that many cases previously described as endothelioma or lymphosarcoma came into this group. He suggested that variations in the local supply of lymphocytes might be a factor in determining the type of tumour.

Hauser and Brownwell (1938) did not think that epithelium overlying lymphoid tissue changed in character and classified lymphoepithelioma as a highly undifferentiated form of medullary squamous carcinoma. In their view all epithelial neoplasms arising from the lining membrane of the nasopharynx were medullary squamous carcinomas.

Furstenberg in the same year classified the malignant tumours of the nasopharynx according to the tissues from which they originated thus: (1) carcinoma from epithelium, (2) sarcoma from connective tissue, (3) lymphoblastoma from lymphatic structures and (4) teratoma which may undergo malignant alteration.

The vast majority are squamous cell carcinoma.

Ch'in and Szutu writing from Peiping in 1940 classified lymphoepithelioma as either a dysontogenetic tumour of branchiogenic origin or a neoplasm of lymphoepithelium, the existence of which they accepted unreservedly. They describe 'subvarieties' of

lymphoepithelioma including types showing squamous change, basal cell and columnar cell histology or glandular formation.

Digby et al (1941) list the structures in the nasopharynx which may give rise to tumours namely (1) columnar epithelium lining the upper part of the nasopharynx, (2) stratified epithelium lining the lower part, (3) mucous glands and (4) lymphoid tissue. They found only one case of typical squamous epithelioma and two of lymphosarcoma and considered that the vast majority of tumours in their series were carcinomata derived from columnar epithelium. They did not think that the term lymphoepithelioma should be used unless lymphocytes occurred in distant metastases other than lymph nodes, and had seen no example of this. In 1951 Digby suggested that "serial sections of all the walls of the nasopharynx both in Chinese and Europeans to determine the exact line of demarcation between ciliated columnar and stratified epithelium and to look for glandular elements which might be the starting point of carcinoma is desirable." Martin (1945) found 73 cases of epidermoid carcinoma among 87 malignant nasopharyngeal growths. Five of these were squamous, 42 transitional-celled, 14 lymphoepithelioma, 4 spindle-celled and 8



not classified.

Godfredsen (1947) described the 454 cases which he had collected as being mainly anaplastic tumours of low differentiation, either squamous epithelial carcinoma or reticulum cell sarcoma. One fifth of these were squamous cell carcinoma undergoing cornification.

Simmons and Ariel (1949) adopted Stewart's classification dividing the tumours into (1) epidermoid carcinoma, (2) transitional cell carcinoma, (3) anaplastic carcinoma and (4) an unclassified group. They did not feel a diagnosis of lymphosarcoma was warranted in any of their 150 cases.

Morrison, Hopp & Wu (1949) outlined a method for diagnosis of nasopharyngeal malignancy from cytological studies by smear technique. A tightly wound cotton applicator was introduced through the anterior nares, rubbed over the nasopharyngeal mucosa and slides were made and stained by the modified method of Papanicolaou and Traut. Malignant cells showed an enlarged nucleus, and a nucleolus with abnormal chromatin content. The cell wall was often distorted, indistinct or absent. The presence of clumps of cells was significant. Seven positive smears were obtained from 8 patients with positive biopsies. The one false negative smear

was explained by the fact that the mucous membrane covering the tumour was intact, and no malignant cells were therefore shed on the surface.

Kramer (1950) enumerates from different types of carcinoma which arise in the nasopharynx. (1) squamous cell carcinoma keratinising or non-keratinising from the squamous epithelium lining the posterior and lower parts, (2) transitional cell carcinoma from the columnar epithelium lining the anterior and upper part, (3) lymphoepithelium from the epithelium overlying lymphoid tissues and (4) undifferentiated carcinoma where the parent epithelium cannot be recognised.

Thompson (1951) regarded lymphoepithelioma as an uncommon tumour. Wilson (1954) thought that 90% of nasopharyngeal malignant tumours were squamous celled carcinoma, transitional celled carcinoma, lympho-epithelioma or lymphosarcoma.

Willis (1954) considers that the controversy over the subject of nasopharyngeal neoplasms is largely over names and that all the epithelial tumours should be classified as epidermoid carcinoma. He feels that the appearance in 'lymphoepithelioma' is a perpetuation of the normal structure of the region from which the tumours arise and that they should be classified as anaplastic carcinoma. Scarff (1955) divides the

carcinomas of the nasopharynx into four groups (1) keratinising squamous cell carcinoma, (2) squamous cell carcinoma with early or little keratinisation, (3) transitional cell carcinoma and (4) lympho-epithelioma.



ANATOMY AND HISTOLOGY OF THE NASOPHARYNX.

The nasopharynx is a six sided cavity having a roof, two lateral walls, a posterior wall, an anterior wall and a floor. The roof or vault is bounded by the basisphenoid and basiocciput and slopes backwards and downwards to be continuous with the posterior wall which lies opposite the lower part of the basiocciput and the first two cervical vertebrae. Each lateral wall measures just over an inch each way and presents anterior to its centre the opening of the Eustachian tube at the level of, and half an inch behind, the inferior turbinate. The opening is bounded above and behind by a ridge of cartilage, the tubal elevation and posterior to this is a recess - the fossa of Rosenmüller which extends sideways for half an inch between the tube and the prevertebral muscles. Anteriorly the nasopharynx is bounded by the posterior nares and inferiorly by the soft palate and pharyngeal isthmus these walls being incomplete and lending access to the nose and oropharynx, while the Eustachian tube gives communication with the middle ear.

Collections of lymphoid tissue are found mainly opposite the basiocciput (nasopharyngeal tonsil) and over the tubal elevation but smaller patches of

lymphoid tissue are scattered over the lateral and posterior walls.

The relations of the nasopharynx are superiorly the sphenoid sinus, the cavernous sinus and the pituitary fossa. The fossa of Rosenmüller lies directly below the foramen lacerum and the apex of the petrous part of the temporal bone. The cavernous sinuses lie on body of sphenoid lateral to and separated by fairly thin bone from the sphenoid sinuses. In the lateral wall of the cavernous sinus run the third, fourth, ophthalmic and sixth nerves in that order from above down. The internal carotid artery lies medial to the nerves. The maxillary nerve runs along the lower border of the sinus.

The foramen lacerum lies postero-lateral to the cavernous sinus and is partly overlapped by the trigeminal ganglion. The motor root of V lies below the trigeminal ganglion and runs laterally and slightly forward to pass through the foramen ovale. The maxillary nerve runs forward along the lower border of cavernous sinus separated from the sphenoid sinus only by thin bone. The ophthalmic nerve enters the cavernous sinus, runs in its lateral wall, and divides into three branches which all enter the orbit through the superior orbital fissure.

The mandibular nerve runs from the trigeminal ganglion to the foramen ovale where it unites with the motor root. The abducens nerve enters the middle cranial fossa when it crosses the petrosphenoid joint. It then curves round the lateral side of ascending part of internal carotid and enters cavernous sinus. Having left the sinus it enters the orbit through the superior orbital fissure.

The oculomotor nerve pierces the dura mater of the roof of the cavernous sinus half way along its surface, runs in its lateral wall and divides into two branches which both enter the orbit through the superior orbital fissure.

The trochlear nerve also enters the orbit through the superior orbital fissure.

The facial nerve leaves the skull through the internal auditory meatus in the posterior cranial fossa and is not therefore in close relation to the nasopharynx at this juncture.

The ninth, tenth and eleventh nerves leave the skull by the jugular foramen and the twelfth by the anterior condylar foramen.

Laterally as Trotter has pointed out the mucous membrane surrounding the Eustachian tube is in relation to the levator palati and Eustachian cartilage,



the mandibular nerve and the internal pterygoid muscle. Lateral to the pharyngeal constrictors lies the parapharyngeal space (Burger) enclosed by transverse processes of the upper cervical vertebrae posteriorly and the ascending ramus of mandible and parotid gland laterally, and in this run the ninth, tenth and twelfth nerves. Posterolaterally, behind the parotid gland the ninth, tenth, eleventh, twelfth and cervical sympathetic chains run downwards, and the facial nerve lies postero-medial to the parotid before it enters the substance of the gland.

Posteriorly lie the prevertebral muscles and fascia and the upper two cervical vertebrae. The pharynx is attached to the basiocciput and petrous temporal bone by a thick band of pharyngo-basilar fascia which lies between the pharyngeal muscles and the mucous membrane. Along the lower surface of the base of the skull, the anterior condylar canal, jugular foramen and stylomastoid foramen are posterolateral to the nasopharynx.

Inferiorly the nasopharynx is in relation to the oropharynx and anteriorly to the nose.

Nerve supply. The glossopharyngeal nerve gives sensory supply to the pharynx and soft palate. The motor nerves to the pharynx come from the pharyngeal

plexus, which arises from the vagus probably through fibres of the accessory. In this study it has been taken as being supplied by the vagus. The muscles of the soft palate are also supplied by the pharyngeal plexus. The pharyngeal branches of the vagus arise immediately below the jugular foramen.

Lymphatic drainage. This is commonly cited in the anatomy books as the retropharyngeal lymph nodes. From the speed and frequency with which the glands alongside the external jugular vein are involved in carcinoma of the nasopharynx, there would appear to be direct drainage to these. It may well be that the lymphatics of the lateral part drain to the glands alongside the external jugular vein in the first instance while these which drain to the retropharyngeal lymph nodes come from the posterior part.

Embryology.

In the embryo the pharynx is derived from the endoderm of the anterior end of the foregut. Until the third week of uterine life (Cunningham) it is separated from the ectodermal depression which becomes the mouth by the bucco-pharyngeal membrane which is composed of approximating layers of ectoderm and endoderm. At the third week this membrane ruptures and the pharynx becomes directly continuous with the

mouth. Also at about the third week the pharyngeal wall is converted into a series of arches with corresponding grooves externally and pouches internally, a process analagous to the formation of gills in the lower vertebrates. From the endoderm of the first pouch is derived the lining epithelium of Eustachian tube, middle ear and inner surface of tympanic membrane. The epithelium of the pharynx arises from the second, third and fourth pouches. At the end of the third month of embryonic life lymphocytic aggregations are laid down around the Eustachian tube, dorsum of tongue and dorsal pharyngeal wall. Their appearance is preceded by a proliferation of endodermal cells which invade the subjacent tissue and mingle with the mesodermal cells, with no basement membrane to form a boundary. The mesodermal cells also proliferate markedly and lymphoid tissue first appears in immediate relation to the invading endodermal cells (Le Gros Clark). The exact origin of these lymphocytes is uncertain. They may be developed in situ, derived from the blood stream or be primarily produced in lymph nodes from which they migrate to the nasopharyngeal wall.

Histology. The mucous membrane of the nasopharynx is ciliated psendostratified columnar epithelium



in the upper and anterior part and squamous epithelium in the lower and posterior part. Some authorities believe that the whole nasopharynx is lined by columnar epithelium and that the transition to squamous takes place at the junction with the oropharynx. From examination of the normal Chinese nasopharynx and of the tumours studied in the present series, it seems that the posterior and lateral walls are lined by squamous epithelium in their lower parts, and in the case of the lateral wall, in its posterior part. This epithelium is however of a relatively undifferentiated type, lacking marked keratinisation and presenting a more flattened appearance than does well differentiated epithelium. Overlying lymphoid tissues the epithelium is thinned out and the basal layer is intimately associated with and may be infiltrated by lymphocytes.

Reference. Jamieson's Companion to the Manuals of Practical Anatomy has been frequently referred to in writing this section, as have his Illustrations of Regional Anatomy in making the illustrations.

A STUDY OF THE CLINICAL FEATURES AND OF THE  
PATHOLOGY OF NASOPHARYNGEAL CARCINOMA AS  
SEEN IN SINGAPORE DURING THE PERIOD  
FEBRUARY 1953 TO APRIL 1955.

One hundred and twelve patients with histologically proven carcinoma of the nasopharynx were seen and investigated by the author in a period of twenty seven months. These patients came to the out-patient department, to the Medical or Surgical units, the Ear, Nose and Throat, Eye or Radiotherapy Departments of the Civil General Hospital, Singapore and were thereupon referred to the author. Whenever possible the patients were admitted to hospital for full investigation but a small minority were seen only as out-patients. Histological sections of the nasopharyngeal growths, lymph gland metastases or both were studied and classified by the writer, as well as sections taken from distant metastases and autopsy material where these were available.

Clinical investigations included the taking of a full history and a full clinical examination including examination of the nasopharynx, ears, larynx and retina. Examination of the nasopharynx was made with a nasopharyngeal mirror. In some cases local anaesthesia was used to facilitate this examination but on the

whole a satisfactory view of the nasopharynx was obtained without its use. Digital examination of the nasopharynx both through the soft palate and by introducing a finger behind the palate was an invaluable aid to diagnosis. Radiological examination of the skull, taking both lateral and basal views was carried out in every case. X-Rays were taken of the chest or skeleton where there was reason to suspect metastases. Biopsies of the nasopharyngeal tumours were taken by the Ear, Nose and Throat surgeons and biopsies of the cervical lymph nodes by the writer. Laboratory investigations included a full blood examination and Wasserman Reaction in some cases and estimation of the plasma proteins in a proportion of cases.

Progress was followed by the author in a special out-patient follow-up Clinic.

#### Sex Distribution.

Of the 112 patients 86 (76.8%) were male and 26 (23.2%) female, giving a male:female ratio of 3.3:1.

#### Age Distribution.

The ages varied from 12 years to 69 years, the average age being 42.1 years. Table I shows the age distribution in the different decades and Table II shows this in the form of a graph.



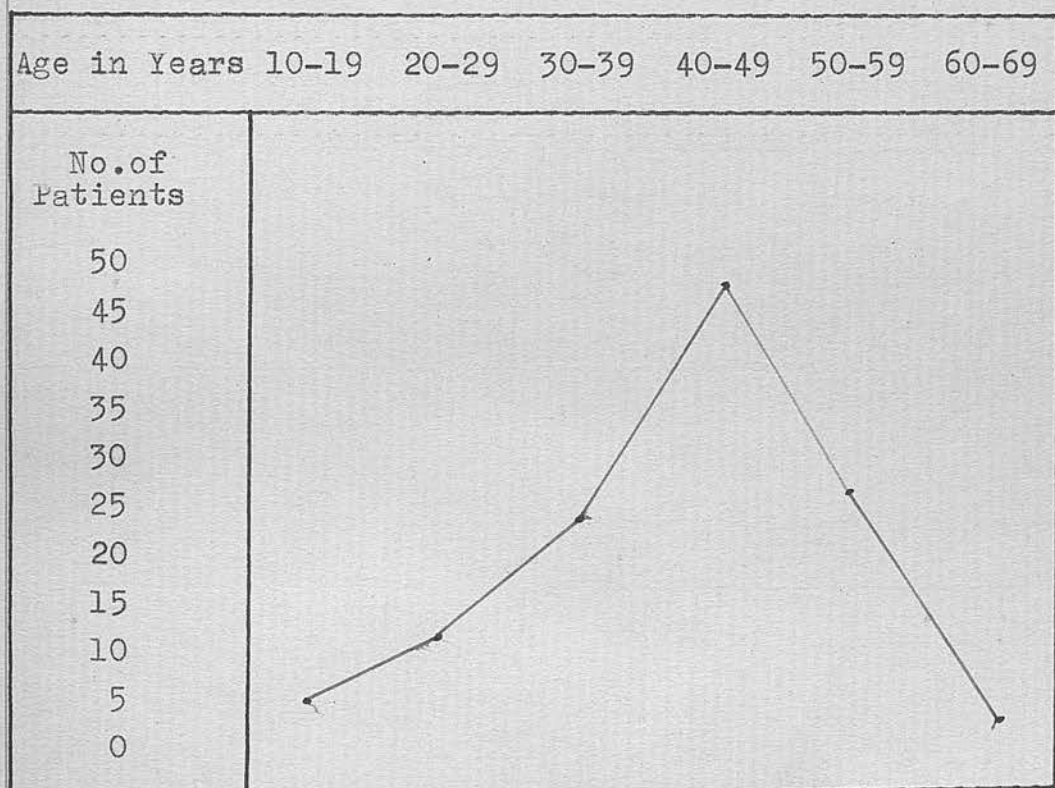
TABLE I.

Age Distribution.

Age in Years	10-19	20-29	30-39	40-49	50-59	60-69
No. of Patients	5	10	23	45	25	4

TABLE II.

Age Distribution.



The average age of male patients (42 years) was slightly higher than that of female patients (40.6 years).

Ethnic Group.

One hundred and seven patients (95.5%) were Chinese, 1 was Eurasian of Chinese extraction - the mother being Chinese and the father half Chinese, 3 were Malay and 1 a Tamil Indian. Of the Chinese 75 (70%) had been born in China, the remainder being born in Singapore (23%), the Federation of Malaya (3%) or Borneo (3%). The Eurasian was born in Borneo, the Malays in the Federation of Malaya and the Indian in India.

All but twelve of the patients were resident in Singapore. The three Malays, three Chinese and the Indian lived in the Federation of Malaya and four Chinese and the Eurasian came from Borneo.

Of the 100 patients resident in Singapore therefore, all were Chinese. Table III gives the relative proportions of the different races in Singapore (Colony of Singapore - Annual Report 1954).

TABLE III.

Population of Singapore.

	No.	%
Total Population	1,165,129	100
Chinese	891,550	76.5
Malay	142,843	12
Indians -Pakistans	91,012	8
Europeans	17,122	1.5
Eurasians	11,402	1
Others	11,200	1

There was therefore a 100% incidence of Chinese among those with nasopharyngeal cancer living in Singapore as opposed to 76.5% of the general population.

Table IV shows the incidence of the disease in the different Chinese ethnic groups of this series as compared with the distribution in the general population.

TABLE IV.  
Chinese Ethnic Groups.

Ethnic Group	Chinese Resident in Singapore in Present Series.		Population of Colony of Singapore (1947 Census) % Total Chinese
	Total No.	% Total Chinese	
Cantonese	30	30	21.6
Hokien	27	27	39.6
Hainanese	14	14	7.2
Hakka	10	10	5.5
Teochew	19	19	21.5
Other Chinese	0	0	4.6

The percentage of Hainanese, Hakka and Cantonese in this series was therefore higher than that of the general population of Singapore while the figure for Hokiens was lower.

Occupation.

This varied greatly, including labourers, rubber tappers,



clerks, shop-keepers, domestic servants, fishermen, carpenters, motor mechanics, teachers and trishaw-riders. The occupations were in fact typical of any cross-section of the poorer classes of Singapore. No one trade or calling seemed therefore to predispose to the condition. In view of the higher incidence of the disease in Hainanese noted above, it is worth noting that all the members of this ethnic group were cooks or coffee-shop owners. The Hakkas and Cantonese however followed a vast number of different occupations.

Religion.

Of the 107 Chinese, 4 were Christian and the others were mainly adherents of Buddhism, Taoism or Confucianism. A few claimed to be "free-thinkers". On careful questioning of the patients it was found that Joss-sticks were burned in nearly every household, if not by the patient by one of his relatives. The burning of Joss-sticks is a custom associated with the ancestral Chinese religions. Joss-sticks may be in the form of small sticks - like firewood; made of sandalwood or of tapers made of material which looks like sandpaper. These are burned in Chinese houses about twice a day, and may take from 5 minutes to half an hour to burn leaving behind them a lingering odour, and varying degrees of smoke.

The Malays were all Moslem, the Indian a Hindu and the Eurasian a Roman Catholic.

Social Factors.

As has been mentioned the vast majority of patients were drawn from the lower social classes, being non-fee-paying patients and having little or no education, only ten of them being able to speak English. The average Chinese home is of a very poor standard, consisting of only one room, which may be shared by two families in the overcrowded urban areas. In many cases the occupants sleep in a series of bunks built against the wall. Cooking and lighting facilities are kerosene stoves and lamps. The diet is mainly of rice, boiled or fried with the addition of local fish, pork and vegetables. These are bought in large open-air markets, the food lying out on tables. The freshness and cleanliness of the food and of its vendors leaves much to be desired, and the European nostril cannot fail to be offended if it enters these markets. The cooking oil in which the food is cooked is used many times over and often has a pungent odour. (The Chinese are not curry-eaters). The general cleanliness of the average Singapore Chinese is of a very low standard.

The Malays and Indians eat mainly meat or fish

curry, rice and vegetables. Those in this series all had good living conditions.

The reluctance of patients to seek Western medical attention or to go to hospital may be noted here. While this is less than it was formerly especially among the male sex, symptoms are allowed to continue for many months in most cases before a doctor is consulted. The Chinese in particular will tolerate symptoms or signs which would cause Europeans to seek medical attention without delay.

#### Duration of Symptoms.

The duration of symptoms when the patient was first seen was 12.8 months on the average, the shortest history being one month and the longest five years. The patient with a 5 year history had had three operations for removal of the glands of the neck, followed each time by recurrences. In general those who had histories of long duration had first noticed lymphadenopathy and this had persisted as the solitary symptom for some time. Many patients had first tried Chinese medicine, mainly in the form of ointments applied locally to the neck glands, and only after these methods had failed or had made the condition worse, did they seek Western methods of treatment. Twenty three patients had a history of over 2 years.



Of these three had initially complained of epistaxis, 2 of headache and the remainder of enlarged glands in the neck. One patient who had suffered from epistaxis for four years, had had three operations performed by an Ear, Nose and Throat surgeon before the correct diagnosis was reached.

TABLE V.  
Initial Symptom.

Symptom	No. of Patients	% of Patients
Enlarged Neck Glands	61	54.4
Epistaxis and/or Nasal obstruction	27	24.1
Ear Symptoms	11	9.8
Headache	12	10.7
Symptoms referable to Cranial Nerves	11	9.8
Sore Throat	1	.9

In five cases nasal symptoms and ear symptoms occurred simultaneously. In a further four cases the initial symptoms were multiple, all having glandular enlargement, combined with epistaxis in two cases, headache in one and blurred vision in another.

Presenting symptom.

This was by no means identical with the initial

symptom of the disease as the patients often tolerated the disease until increased severity of symptoms, particularly pain visual disturbances, or a multiple collection of symptoms gradually wore down their resistance or until they were unable to work and were in financial difficulties.

The frequency of the different presenting symptoms is given in Table VI.

TABLE VI.  
Presenting Symptom.

Symptom	No. of Patients	% of Patients
Enlarged Neck Glands	38	33.9
Headache	13	11.6
Epistaxis	15	13.4
Symptoms due to Cranial Nerve lesions	35	31.3
General Weakness	7	6.3
Symptoms from distant metastases	3	2.7

In addition one patient was brought in by the police in a semiconscious condition having collapsed in the street. This patient was grossly emaciated and the disease was far advanced.

Of the cranial nerve symptoms, visual disturbances,

pain in the distribution of the trigeminal nerve and dysphagia were the chief presenting symptoms. The symptoms due to metastases, comprised lumbar pain in one instance, pain in the shoulder in one, and haemoptysis in a third.

Involvement of the Cervical Lymph Nodes.

Ninety two (82.1%) patients complained of swelling in the neck when they were first seen, and in 12 cases the swelling was said to have appeared on both sides of the neck simultaneously. In all, 46 patients gave a history of bilateral glandular enlargement. The history was of a small swelling appearing behind the angle of the jaw, increasing gradually and usually painlessly to involve a greater or smaller part of the neck. Occasionally the lymph nodes were said to have enlarged suddenly after an initial period of slow growth and in this case the enlargement might be accompanied by pain. The glandular mass had broken down, in some cases, remaining unhealed or bearing scars, following the application of Chinese ointments. The average duration of history of glandular involvement was 11 months and it was therefore an early feature of the disease.

On examination 98 (87.5%) patients exhibited cervical lymphadenopathy when they were first seen and



four others developed it later in the disease. The enlargement was bilateral in 67 cases. Where the involvement was unilateral, it was on the right side in 17 cases and left sided in 14.

The lymphadenopathy varied from a small discrete node palpable below and behind the angle of the mandible to a massive enlargement occupying the whole of one or both sides of the neck, from the mastoid to the clavicle and down the anterior border of trapezius and sometimes extending over the midline anteriorly or posteriorly. The earliest and most common finding was enlargement of glands below and behind the angle of the mandible, and this spread to involve the neighbouring glands of the upper deep cervical group. The anterior triangle was the commonest site of lymph node metastases but later a chain of glands might become palpable down the posterior border of sternomastoid, or a larger glandular mass be palpable in the posterior triangle. In character the lymph nodes were hard, but not "stoney-hard". As more glands became involved a nodular mass was formed, the nodules being bound together by very firm, rubbery like tissue. The glands early became fixed to each other and to the deeper tissues by this firm tissue, a point which became

all too evident when one was taking biopsy specimens from the neck. Fixation to the skin occurred as a late feature or after the use of local ointments. The glands were rarely painful. In 31 cases only small discrete glands were present. In 39 a moderate sized mass was felt and in 26 the glandular enlargement was gross.

#### Nasopharyngeal Symptoms.

Eighty four patients in all (75%) had epistaxis and/or nasal obstruction. One felt a 'lump behind his nose'. In 50 cases epistaxis and nasal obstruction were both present, epistaxis occurring alone in 26 cases and nasal obstruction by itself in only 6.

The duration of symptoms was 7 months on the average for epistaxis and 6 months for nasal obstruction - these symptoms occurring therefore roughly 6 months after the onset of disease.

Epistaxis generally took the form of a fairly frequent loss of small amounts of blood. Occasionally severe epistaxis occurred. Nasal obstruction was frequently complained of as being present or worse in the mornings.

A frequent complaint of inability to smell was also encountered always in conjunction with other nasopharyngeal symptoms.

### The Primary Nasopharyngeal Tumour.

A tumour was found in the nasopharynx of 100 (89.3%) patients. In one of these the growth was not detectable for 6 months after he was first seen, and in another growth was evident four months later. In the others the growth was found either at the time of or within a matter of weeks from the patient's first presentation at hospital.

The tumours fell into two types (1) a fungating exophytic type where the growth projected into the cavity of the nasopharynx, sometimes depressing and paralysing or projecting below the soft palate. In one case it had ulcerated through the soft palate. Occasionally the growth protruded through the posterior nares into the nose. In some cases the growth occupied a large part of the nasopharynx, in others it was a smaller polypoid mass. Many of the large growths were soft and friable and tended to bleed on digital examination. The smaller ones were firmer. Most were irregular, nodular or lobular, and some were ulcerated superficially. (2) A small lesion which did not project into the cavity of the nasopharynx and which was commonly felt as a slightly raised, hard plaque in the nasopharyngeal mucosa, usually ulcerated superficially. Occasionally a vague



induration or roughness was palpable in the nasopharynx. Table VII shows the proportion of tumours in each of the two types.

TABLE VII.

Type of Nasopharyngeal Tumour.

	Total No.	% of Primary Growth
Fungating Type	70	70
Small ulcerating Type	30	30

The site of origin of these tumours was (1) the lateral wall especially in the region of the Eustachian tube and the fossa of Rosenmüller i.e. more in its posterior than in its anterior part, (2) the posterior wall, mainly towards its centre or (3) the nasopharyngeal vault usually near the choanae.

Table VIII shows the distribution of the nasopharyngeal tumours with regard to site, and of the relation of type of tumour to site.

TABLE VIII.

Site of Nasopharyngeal Tumours.

	Lateral Wall		Posterior Wall		Roof	
	Total	% of Total Growths	Total	% of Total Growths	Total	% of Total Growths
Total No.	62	62.6	21	21.2	15	15.2
Fungating Lesions	40	-	15	-	13	-
Small Lesions	22	-	6	-	2	-

One tumour (1% of total growths) occupied almost the whole nasopharynx and it was not possible to discover its site of origin. Nearly two-thirds of all tumours therefore arose from the lateral wall and of these 64.5% were fungating in type and 35.5% small ulcerative lesions.

The tumours of the posterior wall comprised one-fifth of all nasopharyngeal tumours and of these 71.4% were fungating and 28.6% small.

In the roof where 15% of all tumours arose, 86.7% were fungating and 13.3% small.

Tumours arose from the right side in 50 cases, from the left in 43 and from the centre (of the posterior wall) in 6.

### Ear Symptoms.

Seventy six patients (67.9%) had symptoms referable to the ear, and in all but one these symptoms were present when the patient was first seen. The ear symptoms were multiple in 46 of these cases and included deafness, tinnitus, aural discharge and pain in the ear. The commonest combination of symptoms was deafness and tinnitus (31 cases) in some of which a discharge was present as well. The ear symptoms were bilateral in 9 instances. In all but 11 cases the ear symptoms were accompanied by nasopharyngeal symptoms. The average duration of symptoms referable to the ear was 6 months - thus corresponding closely with the average time of appearance of nasopharyngeal symptoms. Deafness was not accompanied by vertigo or vestibular disturbances in any case.

On examination, the tympanic membrane was opaque and rather pale-looking with retraction of the drum head in 10 cases. Also in 10 cases discharge was present, purulent in one, blood-stained in another the remainder being serous. In all of these the drum was perforated. Fifty seven patients were found to be deaf but Rinne's test was not positive in any one of them.



### Headache.

Eighty patients (71.4%) complained of headache, the average duration of pain being 5 months. The site of pain was commonly in the temple (39 cases). Less frequent sites were the frontal region (9) occipital area (7) parietal region (6) over the vertex (3) and in 16 cases there was generalised pain. Headache was bitemporal in 8 cases and bifrontal in three. The pain was usually fairly constant and a dull rather than a neuralgic pain. In many cases it was extremely severe, the patient could talk or think of nothing else and in some cases a prefrontal leucotomy was necessary to relieve the suffering.

### Cranial Nerve Lesions.

Symptoms referable to the cranial nerves were given by 66 (59%) patients. The first symptom appeared on the average 8.6 months after the onset of disease. In 11 cases a cranial nerve symptom was the initial one.

The main symptoms referable to the cranial nerves and the average length of time after the onset of disease at which they appeared are listed in the following table.

TABLE IX.  
Cranial Nerve Symptoms.

Symptom	No. of Cases	Average time of appearance after onset of disease in months.
Blurred vision	35	12.5
Diplopia	15	12.5
Total blindness of one eye	5	25
Squint	9	14.5
Ptosis	6	9
Pain in distribution of V	26	6
Numbness do. do. do. do.	8	3.5
Inability to clench jaw	5	9.5
Facial asymmetry	4	7
Dysphagia	9	15
Hoarseness	9	13

Numbness or pain in the branches of the trigeminal nerve (mainly the maxillary nerve) were therefore the earliest cranial nerve symptoms to appear but visual disturbances which arose slightly later composed the largest group of symptoms. Blurred vision and diplopia frequently occurred together and blindness was always preceded by other visual disturbances. Dysphagia occurred in 30 patients altogether but where there were grossly enlarged lymph nodes and/or a large

nasopharyngeal tumour its presence was not attributed to a cranial nerve lesion.

On examination the cranial nerves were involved in 71 cases (63.4%). The individual nerves were involved with the following frequency -

TABLE X.  
Cranial Nerve Lesions.

Nerve	Total cases involved	Involved with other nerves	Involved alone	Accompanied by Cranial Involvement
II	6	6	-	6
III	20	19	1	19
IV	6	6	-	6
V	40	33	7	28
VI	30	27	3	24
VII	8	8	-	8
IX	4	3	1	3
X	30	25	5	24
XI	26	24	2	16
XII	21	21	-	16
Cervical Sympathetic	4	4	-	3

Cranial nerves were therefore involved in the following order of frequency, V, VI and X, XI, XII, III, VII, IV and II, IX and the cervical sympathetic. The lesions were multiple in all but 19 cases. The



second, fourth, seventh, twelfth and cervical sympathetic nerves were never involved alone. The following is a description of the signs of cranial nerve involvement seen in this series.

The olfactory nerve could never be assessed because of the frequency of anosmia due to nasal obstruction. The signs of involvement of the optic nerve were total blindness in all cases, accompanied by optic atrophy in 3 cases, papilloedema in 2.

Oculomotor lesions fell into two categories (a) ptosis and (b) abnormalities of the pupillary reflexes. Ptosis occurred in 15 cases and in 4 of these was associated with absence of light and accommodation reflexes. Absent reflexes were present without ptosis in 5 cases. Two patients developed bilateral ptosis in the late stages. In one case there was an external squint, in most cases ophthalmoplegia due to oculomotor lesions were accompanied by lesions of VI and sometimes IV and the eye therefore remained almost central. Complete ophthalmoplegia occurred in 4 cases.

Trochlear nerve lesions never occurred alone and were always associated with third or sixth nerve lesions and the signs were dependent therefore on the accompanying lesions.

Trigeminal nerve involvement was the commonest sign

of cranial nerve damage. The frequency with which its different branches were affected is given in Table XI.

TABLE XI.  
Trigeminal Nerve Lesions.

Division of V.	Involved Alone	Involved with other Branches of V.	Involved with nerves other than V.	Total	Number with Cranial Involvement
Ophthalmic	-	11	1	12	12
Maxillary	5	17	7	29	23
Mandibular	1	13	-	14	12
Motor	2	10	8	20	16

Ophthalmic nerve lesions were demonstrated by (1) neuralgia hyperaesthesia or numbness over the skin of the median part of the nose, the upper eyelid, forehead and scalp up to the vertex, (2) pain in the eye itself, (3) an absent corneal reflex or in the late stages as the result of this corneal ulceration and keratitis might occur. The corneal reflex was absent in 5 cases, and two of these later developed keratitis.

Maxillary nerve involvement was indicated by pain or sensory impairment over the area bordered by the side of the nose, the upper lip, the lower eyelid and

a line drawn from the angle of the mouth to the middle of the temporal ridge.

Manibular nerve injuries caused signs of neuralgia, hyper or hypoaesthesia over the lower lip and chin, lateral part of the cheek, the ear or the temple.

Signs of involvement of the motor division was shown by wasting of the masseter or temporalis muscles, and by a deviation of the jaw to the side of the lesion on clenching the teeth.

Abducens nerve lesions produced an internal squint with inability of the eye to look outwards. Diplopia and blurred vision were concomitant symptoms.

Lesions of the facial nerve manifested themselves by weakness or occasionally by fibrillary tremor of the facial muscles. The lesion was always of the lower motor neurone type. The eighth nerve was never involved.

Signs of glossopharyngeal paralysis were taken as sensory loss of the soft palate or posterior third of the tongue. The signs of involvement of the tenth nerve present a little more difficulty. There is still some disagreement about the innervation of the palate, but most authorities agree that it is supplied by the vagus through fibres of the spinal



accessory nerve. Russell Brain includes palatal paresis under vagus lesions and so it has been classified here. Where there was obvious depression or infiltration of the soft palate by tumour it was of course not included among vagal lesions. The paralysis was noted by a failure of elevation of the palate, and by deviation of the uvula to the opposite side on saying "ah". Where dysphagia existed, in the absence of markedly enlarged glands or a large nasopharyngeal tumour protruding below the palate into the oropharynx, this was also taken as a vagus injury, due to paralysis of the superior constrictor. Dysphagia was always for solids and only in a few very advanced cases was there inability to swallow fluids. Paralysis of the vocal cord was the third sign of vagus injuries.

The eleventh cranial nerve lesions were demonstrated by paralysis of the sternomastoid and/or trapezius muscles. Hypoglossal nerve injuries were shown by atrophy of the tongue on the side of the lesion and deviation of the tongue to the same side on protrusion.

The lesions of the cervical sympathetic produced Horner's syndrome shown by enophthalmos and a constricted pupil. Several neurological syndromes have

been cited in describing the cranial nerve lesions produced by nasopharyngeal carcinoma. Burger has emphasised the weakness of classifying the lesions in this manner as one syndrome may progress to another in a short period of time due to involvement of further nerves. The syndromes however will be briefly summarised and their frequency in this series indicated.

(1) Jacod's petrosphenoidal syndrome where there is unilateral neuralgia of the trigeminal nerve and total unilateral ophthalmoplegia due to involvement of II, III, IV and VI. This occurred in 4 cases.

(2) Gradenigo's syndrome due to lesions at the tip of the petrous temporal bone causing ocular palsy (usually VI) with pain in the distribution of V. This was seen 9 times.

(3) Godtfredsen's syndrome of ophthalmoplegia, usually of VI combined with a lesion of XII. This occurred twice.

(4) The syndrome of the jugular foramen, where IX, X and XI are involved. This syndrome was not encountered in that precise form.

(5) Syndrome of the retroparotidean space, giving lesions of IX, X, XI, XII and of the cervical sympathetic. This occurred twice.

(6) Collet described a syndrome similar to (5) but

where the sympathetic escaped. This was seen once.

(7) The syndrome of the paropharyngeal space where there are lesions of IX, X and XII. This occurred once.

(8) The syndrome of Hughlings Jackson where X, XI and XII are involved. This was demonstrated in 5 cases.

Apart from these classical syndromes which are largely a matter of historical interest, there are two groups of cranial nerve lesions to which attention is drawn. These are firstly, involvement of the nerves of the cavernous sinus, namely the abducens, ophthalmic, trochlear and oculomotor nerves, and in addition to these the maxillary nerve which runs along the lower border of the sinus. One or more of these nerves were involved in 48 (42.9%) of cases. The most commonly involved was the abducens nerve (30) and the maxillary nerve (29). These were involved together in 18 instances.

The ophthalmic and trochlear nerves were never involved without an accompanying paralysis of either the maxillary or abducens nerve or both. The oculomotor nerve was involved by itself in only one instance, and in all the others, another nerve of the cavernous sinus was involved. Another point to note is that the optic nerve was never involved until



late in the disease and never without previous signs of injury of the nerves of the cavernous sinus. The second group of nerves to which it is desired to call attention are the four last cranial nerves and the cervical sympathetic. All manner of combinations of lesions of these five nerves were encountered, and some or all of them were involved in 47 cases, in 19 of which more than one nerve was affected.

Bilateral cranial nerve lesions occurred in 10 cases.

In all except one case the lesions were unilateral when first seen and further lesions appeared on the other side later in the disease.

One patient (case 84) had bilateral ptosis and bilateral ophthalmoplegia when he was first seen. The right eye was central and could move a fraction laterally, the left eye remained central and moved in no direction. He complained of blurred vision but was not blind and examination of the retina revealed no abnormality.

In all, 47 patients, that is 66.2% of those with cranial nerve lesions had radiological evidence of involvement of the base of the skull. Thirty nine (81.2%) of these with lesions of the nerves in the cavernous sinus showed cranial involvement on X-Ray and lesions of the last four cranial nerves showed

this feature in 28 (59.6%) of cases. Of the 10 cases in which one or more of the last four cranial nerves was involved, and in which there was no lesion of the other cranial nerves only one showed erosion of the skull.

One patient complained of severe 'itchiness' of one eye, and gave a history that tears had flowed from this eye for a period of weeks before he was seen. This was the only case in which there was any indication of involvement of the nerve of the pterygoid canal.

#### Radiological Appearances of the Skull.

In all 71 patients (63.4%) had some abnormality of the skull on X-Ray. These fell into three groups (1) abnormality of the nasopharynx, (2) involvement of the base of the skull and (3) metastases in the cranial vault.

(1) Thirty nine patients showed some abnormality of the nasopharynx on X-Ray. Twenty two of those demonstrated thickening of the post-nasal wall which could be seen on a lateral view of the skull. Seventeen had a soft tissue swelling in the nasopharynx, which could be vaguely discerned on a lateral view but which became evident on the basal projection of the skull when the normal air-space indicating the nasopharynx

was filled in part or whole by a slightly opaque mass. In one of these tumour could be seen in the nasal cavity.

(2) The base of the skull was involved in 59 (52.7%) cases.. The involvement was nearly always destructive, proliferative changes being present in only 2 cases. The main site of erosion was the middle cranial fossa, in its middle part. The bones involved are the body of sphenoid, the medial part of the greater wing of sphenoid, and the apex of the petrous part of the temporal bone. There was erosion of the middle cranial fossa in 49 cases. In 8 cases all the landmarks of the middle cranial fossa were lost, except for its most lateral portion, and in one of these the destruction was bilateral. The body of sphenoid was partially destroyed in 21 cases, the medial margin of the greater wing in 12 and there was erosion at the petrous apex in 28 cases. The basal foramina particularly the F. lacerum and less commonly F. ovale were frequently enlarged.

The sella turcica was eroded in 10 cases, in four of which the posterior clinoid processes had completely disappeared.

The sphenoid sinus was invaded by tumour as shown by an opacity on the X-Ray film in 19 cases.



The ethmoid sinuses were opaque in 2 cases.

There was erosion of the basiocciput in 5 cases.

In two cases there was a sclerotic region in the middle cranial fossa, both in the adjoining part of the sphenoid bone to the petrosa.

(3) The vault of the skull was the site of metastases in 5 cases. All the metastases were osteoporotic. This appeared at a late stage of the disease.

Other skull changes which were encountered were a swelling in the orbit in one case, erosion of the posterior wall of the orbit and the structures of the nasal fossa in another.

#### Distant Metastases.

Symptoms from distant metastases occurred in 24 patients. These occurred on the average 17.3 months after the onset of disease. Distant metastases were detected on clinical, radiological or autopsy examination in 33 (29.5%).

The symptoms due to metastases fell into certain main categories.

(1) Pain which was the most common symptom. This was situated in the lumbar region in 9 cases, in the chest in 5, in the legs, shoulder, hip, sacrum and epigastrium in one case each.

(2) Cough, Haemoptysis and Dyspnoea. Cough occurred

as a symptom in 8 cases, in 5 was accompanied by haemoptysis, in 3 by dyspnoea. Dyspnoea occurred once in association with pain in the chest.

(3) Ataxia. Six patients complained of weakness of their legs, followed by stiffness and increasing difficulty in walking. Three of these patients developed Retention of urine.

(4) Swellings in various sites were another feature of which patients complained. One man had a swelling of his sternum when he was first seen - one woman had swelling of her shoulder, and a third patient had swellings in the chest.

On clinical examination there was enlargement of the liver in 5 cases, the liver having an irregular, hard border which was tender on palpation. One of these patients had gross ascites and peripheral oedema. The 6 patients who developed spastic gaits showed the signs of a pyramidal tract lesion, with extremely brisk tendon reflexes, an extensor plantar response, and clonus. One developed a sensory level at the 6th dorsal vertebra, and one at the 10th dorsal vertebra. In one patient there was a hard mass arising from the manubrium sterni - fixed to and continuous with bone. In another the whole of one shoulder was greatly enlarged with tumour, which was nodular, firm

rather than hard over most of its surface, cystic in one place, and agonisingly tender on palpation.

A fixed hard mass was palpable over the iliac crest in one case. A further case had two tumours of the chest wall, hard and painless in character, overlying and fixed to the fourth and seventh ribs respectively. Two patients had palpable nodules of the cranium.

Radiological examination revealed many more metastases. These were osteoporotic lesions except for one sclerotic deposit in the 6th dorsal vertebrae. In one case the shoulder joint and acromioclavicular joint were completely destroyed. The presence of further metastases were demonstrated at post mortem in 5 cases.

Table XII indicates the frequency with which metastases occurred in various sites.

TABLE XII./



TABLE XII.

Distant Metastases.

Site	Number of Cases.
Lungs	9
Liver	8
Suprarenal Gland	1
Lumbar Spine	4
Dorsal Spine	6
Cervical Spine	2
Sacrum	3
Pelvis	4
Femur	2
Humerus	2
Clavicle	2
Sternum	1
Ribs	9
Vault of skull	5
Cerebro-pontine angle	1

The most common sites of metastases were therefore the lungs, ribs, liver and dorsal vertebrae.

Other Clinical Features.

Trismus was present in 17 cases. The patient complained of inability to open the mouth, usually occurring about 6 months after the onset of disease. In some cases trismus was so severe that examination of the nasopharynx was impossible, the patient being

unable to open the mouth more than half an inch.

In severe cases feeding also became a problem.

Exophtalmos was noted in 6 cases. All had numerous cranial nerve lesions and erosion of the base of the skull.

#### Axillary Lymphadenopathy.

This occurred in seven cases, always as a late sign of disease. The lymph nodes were fixed, nodular and rubbery hard, and were always associated with gross enlargement of the cervical glands. The inguinal lymph nodes were enlarged in several cases but their character was never truly characteristic of malignancy and no neoplastic change was seen on removal of any inguinal nodes removed for biopsy.

#### General Condition.

The general condition was not good on the whole but neither is that of the average lower class Chinese. Ten patients were markedly emaciated when they were first seen.

#### Laboratory Data.

Apart from a mild degree of anaemia, there was no abnormality in the blood count of these patients. Three patients developed anaemia of such severity as to necessitate blood transfusion.

The Wasserman reaction was negative in all but three cases.

A reversed albumin-globulin ratio was found when the plasma proteins were estimated in one patient and thereafter routine estimation was instituted. In all, 14 out of 30 patients had a raised globulin fraction in relation to the albumin fraction. Routine tests of hospitalised patients without cancer or severe disease (e.g. patients who were admitted for herniorrhaphy) did not show any alteration in the albumin-globulin ratio. This investigation however was not carried out in a sufficient number of cases of nasopharyngeal carcinoma to allow any conclusions to be made.



### PATHOLOGY

The gross pathology of the nasopharyngeal tumours and of their regional metastases, has already been described. In studying the histology of the tumours in this series and of the nasopharyngeal tumours or lymph node metastases of nearly a hundred other cases of nasopharyngeal carcinoma where the patients were not personally seen by the author, it became evident that the neoplasms fell into three groups. Histological classification was therefore made on the basis of division into the following three groups:-

#### GROUP I.

##### Differentiated squamous cell carcinoma.

While tumours which showed keratinisation and the formation of epithelial pearls comprised this group, no case was seen of a fully differentiated cornifying squamous epithelioma of the Broders Group 1 type.

#### GROUP II.

An Intermediate Group of tumours including non-keratinising squamous epithelioma and transitional cell carcinoma. In this group were included all squamous epitheliomata in which cornification and cell-

nest formation were absent, but in which prickle-cell formation was present to a greater or lesser extent and all tumours whose origin from surface squamous epithelium could be traced. The origin from squamous epithelium could be seen to be multifocal in most instances and in the vast majority of cases the neoplastic process appeared to originate in the cells near the base of the epithelium. Also included in this group were tumours presenting the appearance of transitional cell carcinoma, i.e. solid groups of cells with scanty cytoplasm and hyperchromatic nuclei. At first an attempt was made to differentiate squamous cell carcinoma of a low grade of differentiation and transitional cell carcinoma but in many cases the borderline was so slight and the appearances in different parts of one tumour so variable, that it was impossible to decide to which subgroup a particular tumour belonged. Further the cytology of many tumours which arose from the surface squamous epithelium gave the appearance of transitional cell carcinoma. In all tumours of this group mitosis was frequent. The typical appearance of the intermediate group of tumours was of irregular epithelial masses of closely packed cells, set in a fibrovascular stroma containing lymphocytes and plasma cells. Example of transitional

cell carcinoma which arose from the columnar epithelium were seen.

### GROUP III.

Anaplastic Carcinomata. In this group were included the lymphoepitheliomata and anaplastic carcinomata with no obvious origin from surface epithelium and which lacked infiltration by lymphocytes. The lymphoepitheliomata were composed of masses of anaplastic epithelial cells, with scanty ill-defined cytoplasm and large vesicular nucleus containing dark staining nucleoli, with invasion of the tumour masses by lymphocytes. The cells were arranged in cords or columns between which lymphocytes were present but in most cases the columns were packed against one another so that a large mass of tumour cells was seen. In a few cases the tumour cells were loosely arranged or scattered with lymphocytes between them but this was the exception. The epithelial cells of the anaplastic carcinomata resembled those of lymphoepithelioma but there was no lymphocytic infiltration of the tumour masses. The stroma of lymphoepithelioma always contained a great number of lymphocytes and plasma cells and was less dense than that of the Group I or Group II lesions.



Sections from the nasopharynx and/or the lymph node metastases of 111 patients in this series were examined. The sections were routinely stained with haematoxylin and eosin. The remaining patient was diagnosed as "Lymphoepithelioma" by a pathologist in the Federation of Malaya.

Where no primary nasopharyngeal tumour was detected and only a biopsy specimen from a cervical lymph gland was available, this was only accepted as secondary to an undiscovered carcinoma of the nasopharynx if there was good clinical or radiological evidence to support the diagnosis.

The tumours fell into the three histological groups in the following proportions:-

Group I.	Differentiated squamous cell carcinoma		
	Total	3	Percentage 2.7
Group II.	Intermediate Gp of carcinoma		
	Total	76	Percentage 68.5
Group III.	Anaplastic carcinoma		
	Total	32	Percentage 28.8

The distribution of the three groups with regard to the macroscopic type of primary growth is shown in Table

XIII. In twelve cases no growth was found in the nasopharynx, but of these a positive biopsy was obtained from the nasopharynx in one patient.

TABLE XIII.

Relation of Macroscopic and Microscopic Pathology

	Fungating Lesion		Small Lesion		No Lesion	
	Total	% of Hist. Group	Total	% of Hist. Group	Total	% of Hist. Group
Gp I	-	-	2	66.7	1	33.3
II	50	66	20	26	6	8
III	19	59.4	8	25	5	15.6

The percentage of each type of primary growth which fell into each histological group is shown in Table XIV.

TABLE XIV.

	% of Fungating Lesion	% of Small Lesion
Group I	-	6.7
Group II	72.5	66.6
Group III	27.5	26.7

The relation of histological group to site of origin of tumour is shown in Table XV.

TABLE XV.

Relation of Histological Group to Site

	Roof	Posterior Wall	Lateral Wall	Total
Group I	-	-	2	2
Group II	12	13	44	69
Group III	3	8	16	27
Total	15	21	62	

Lymphoepithelioma although it has been included in Group III lesions must be mentioned separately. Twelve tumours showed a histological picture of lymphoepithelioma. Macroscopically seven were fungating, three ulcerating and in two no tumour was found in the nasopharynx. Two arose from the posterior wall, two from the roof and six from the lateral wall.

Table XVI shows the clinical behaviour of tumours of the three groups.

TABLE XVI.

Relation of Histology and Clinical Features

	Cervical Adenopathy		Cranial Nerve Lesions		Distant Metastases		Alive		Dead	
	Total	%	Total	%	Total	%	Total	%	Total	%
Gp I	2	66.7	1	33.3	1	33.3	-		1	33.3
II	67	88.2	58	76.3	26	34.2	28	36.8	16	21
III	32	100	13	40.6	5	15.6	16	50	7	21.9

(The percentage in this table refers to percentage of each histological group which present a clinical feature).

It is therefore seen that the more anaplastic a tumour becomes the greater the incidence of lymph node metastases. The intermediate group accounted for



four-fifths of cranial nerve lesions. Erosion of the middle cranial fossa without cranial nerve involvement was present in 10 Gp. II lesions. As the figures for follow-up are incomplete due to the large number of cases whose progress was unknown, they cannot be regarded as of great significance but the prognosis for Gp. III lesions does appear better than for more differentiated tumours.

Post Mortem Examination was carried out in seven cases (Cases 3, 11, 19, 27, 40, 50 and 62). Unfortunately autopsy examination was hard to secure, not only because permission was refused, but because of a reluctance on the part of the Chinese to die in a Western Hospital, which resulted in many patients being taken home by their relatives shortly before they died.

The findings in all seven cases are summarised here.

Case 3. Chinese Cantonese Male aged 42.

A fungating tumour arising from the lateral nasopharyngeal wall was present on clinical examination. The day before death the patient became suddenly dyspnoeic and cyanosed and breathing was obstructed. He died the following night. Histologically the tumour was an anaplastic carcinoma without lymphocytic

infiltration. At autopsy the mucosa of the entire nasopharynx was reddened and oedematous. There was an ulcer at junction of roof, posterior and lateral walls on the right side. The sphenoid sinus was filled with soft yellow-white tumour which had invaded the surrounding bone. The whole right side of the neck was occupied by enlarged lymph nodes which were firm, and yellowish-white on section. The conclusion was that the friable and fungating nasopharyngeal tumour had broken off and been aspirated by the patient causing obstruction to the air passages. The lungs were uniformly congested but no secondaries were found. Histological examination of the nasopharyngeal ulcer lymph node metastases and the bone at the base of the skull revealed masses of epithelial cells with scanty cytoplasm, with spindle shaped nuclei, mainly vesicular but in some parts darker staining. No lymphocytic infiltration was noted. A reticulum stain showed the cells to be in alveolar groups separated by fibrous bands.

Case 11. Chinese Cantonese Male aged 42.

The patient had presented with visual disturbances and severe headache of  $3\frac{1}{2}$  months duration, a raised indurated tumour was felt in the nasopharynx. A prefrontal leucotomy was performed, and he died the

following day. Histologically a tumour arising from squamous epithelium, composed of solid masses of cell with hyperchromatic nuclei, and of some "prickle-cells" was seen. At post mortem the walls of the nasopharynx were irregular, nodular and thick and section showed irregular submucous tumour infiltration and intracranial extension with small flat deposits in the anterior and middle cranial fossae. Histological examination of post mortem specimens from the nasopharynx and base of skull confirmed the previous findings.

Case 19. Chinese Hakka Male aged 37.

The patient was first seen with a two years history of epistaxis followed by numerous other symptoms. A soft friable mass was seen arising from the lateral nasopharyngeal way and multiple cranial nerve lesions were present. Histologically the primary tumour was an undifferentiated squamous cell carcinoma. Later he developed lymph node metastasis and a deposit in the neck of the femur. He deteriorated rapidly and was readmitted to hospital 8 months after he was first seen, while having palliative X-Rays to his femoral metastasis. Two months later, having continued to deteriorate, he became dyspnoeic and unconscious and his temperature rose suddenly to 106°. He died the same night.



At post mortem a huge nasopharyngeal tumour and lymph node metastases was present. A tumour mass firm and white in character were present at the cerebro-pontine angle and this had eroded through the dura and the base of the skull. Section of the cerebro-pontine angle tumour showed similar histology to that of the primary tumour.

Case 27. Chinese Hakka Male aged 44.

Clinically there was a smallish nodular tumour projecting from the lateral nasopharyngeal wall, bilateral cervical adenopathy and lesions of V, IX, X and XII on the left side. Histologically the tumour presented the appearance of transitional cell carcinoma. He shortly developed sciatic pain and erosion of the right sacro-iliac joint was seen radiologically. He died one month later. On autopsy examination a nodular tumour which had ulcerated superficially was found arising from the lateral wall of the nasopharynx. The cervical lymph node of both sides were markedly enlarged and were firm and white on section. There was a fibrinopurulent exudate on the pericardium and the pleural surfaces of the lower lobe of both lungs. The pericardial cavity was distended with greenish yellow pus. The liver contained irregular whitish nodules both in the subcapsular area and in its

substance. The right first, sixth and seventh ribs and the left fourth, sixth and eighth ribs contained oval secondary tumour deposits which had eroded the bone. Tumour nodules were seen in the middle cranial fosse and petrous bone on the left, invading the dura. Two flat extradural deposits were seen, one in (L) temporal region and another in (R) parietal area. Histological examination of the metastases showed these to be similar to the primary tumour.

Case 40. Chinese Hokier Male age 60.

This patient came to hospital because of dysphagia and hoarseness. He had an eighteen-month history of swelling in the neck. There was an enormous nasopharyngeal tumour and gross adenopathy occupying the whole of the left side of the neck and continuing over the mid line to the posterior border of sternomastoid on the right. X-Ray showed a large soft tissue mass displacing the oropharynx, larynx and trachea to the right. There was erosion of the fifth cervical vertebra.

He became dyspnoeic and had increasing difficulty in swallowing and died two weeks after he was first seen. Histologically the tumour was a Grade 3 (Broder's) squamous epithelioma.

At post mortem the clinical findings were confirmed.

The whole thyroid gland was found to have been invaded by tumour.

Case 50. Chinese Teochew Male age 50.

This patient was found in a collapsed state on the street and brought into hospital by the police. He was emaciated, had a large fungating tumour of the vault of the nasopharynx, gross cervical adenopathy of one side, ptosis and X-Ray evidence of cranial involvement. He was bedridden and rapidly deteriorated, dying one month after admission. At post mortem both pleural cavities contained brownish fluid. Raised plaques of white tumour tissue were adhered to the pleura of the right lower lobe and over the posterior thoracic wall. Small nodules were scattered near the surface of both lungs.

The liver contained numerous white circumscribed round tumour nodules. Both suprarenal glands contained white tumour tissue in the medullary portions.

No invasion was seen at the cranial base.

Histological examination of the nasopharynx, liver, lung and adrenals showed nodules of very anaplastic tumour cells which betrayed their epithelial origin only by small areas of more differentiated epithelial cells.



Case 62. Chinese Teochew Female aged 41.

This woman was first seen with a fourteen month history of nearly all the symptoms to which nasopharyngeal tumours may give rise. A rough patch was felt on the posterior nasopharyngeal wall and bilateral cervical glands were palpable. Histologically the tumour was an undifferentiated squamous cell carcinoma. She was given radiotherapy to which she responded but one month later was readmitted to hospital with paralysis of her legs, retention of urine and faeces. X-Ray showed the bodies of the fifth - sixth dorsal vertebrae to be collapsed. There was sensory loss below the level of D6.

She steadily deteriorated and died two months later. At autopsy numerous large areas of tumour were seen in the liver. They were cystic in consistence and appeared necrotic and haemorrhagic on cross-section.

Tumour tissue was found around the body of the sixth dorsal vertebra.

Study of these cases would suggest that if post mortem examination could be carried out in every case of nasopharyngeal carcinoma who died the incidence of skeletal and visceral metastases would be higher than is at the moment supposed. The cerebro pontine angle

tumour arose as a direct extension of tumour rather than a distant metastasis. The histology of visceral and skeletal metastases imitates that of the primary tumour.

## TREATMENT

### 1. Symptomatic Treatment.

(a) Analgesics. Pain necessitated the giving of analgesics in most cases. For the lesser degrees of pain it was found that Codein was of more value than any other drug. Many patients continued to take Codein for months or years without its effect diminishing. It was given in doses of 10 mgms. three times daily by mouth.

Physeptone and Heptalgin were very badly tolerated and the patients said they felt sick or giddy with these preparations and preferred to return to codein.

For patients with severe pain who were being treated as out-patients Hoyle's Cocktail alleviated the pain in many cases. This was given in 1 oz. doses, 6 hourly. While this was of temporary value, it did not continue to relieve pain for long, possibly because the underlying cause of pain (cranial or distant metastases) was becoming worse. Morphine was given to patients in severe pain who were hospitalised but could not be given at home. Where it was used it had to be given in ever-increasing doses. Its use was confined to patients in whom the disease was advanced



and whose expectation of life was short indeed.

(b) Largactil. Of recent months largactil has been given to patients whose pain could not be relieved by oral drugs and who were living at home, or to patients who were becoming increasingly aware of the severity and ultimate outlook of their condition. Initially largactil was given in a dose of 25 mgms. 6 hourly and this was increased within two weeks to 50 mgms. 6 hourly if necessary. This was taken in addition to an analgesic but the dose of the latter was lowered by half of what the patient had previously taken. While no result was noticed for the first week or so in most cases, after that largactil did have a marked effect in improving the patient's outlook on life, and pain was relieved by a small dosage of analgesic. As this drug was not given until the last few months of the study the duration of its effect cannot be assessed, but its value even if it were only temporary, cannot be denied.

(c) Nasal Decongestants. Nasal drops consisting of  $\frac{1}{2}\%$  ephedrine in normal saline were given to patients with nasal obstruction; but produced only a temporary relief. Inhalations of menthol were found to give longer freedom from symptoms.

(d) In some cases with severe epistaxis adrenaline

packs were introduced through the nose. In addition an injection of 10 ccs. of naphthionine were given and the bleeding was quelled satisfactorily for the time being by these measures.

(e) Soft or fluid diets, had to be provided for many patients with dysphagia. Tube feeding never became necessary but the patient had to be constantly encouraged to swallow.

## 2. Urethane. (Ethyl Carbamate).

Compounds of the carbamate group have been observed to suppress cell-division in plants, bacteria, protozoa and in animal tissues in vitro, to relieve bronchial asthma, to increase the potassium content of bronchial secretion in the cat, to exert a toxic action upon the rat liver and to cause inflammatory lesions in the lungs of mice. Urethane has also been used as an anaesthetic in animal experiments for many years.

The first experiments in the use of urethane upon animal tissues in vivo were carried out by Haddon and Sexton (1946) who found that growth was suppressed in the Walker Rat carcinoma 256. They found that there was a modification in the cellular structure of the tumour, and suggested that this was due to an attempted differentiation of the tumour cells. Paterson et al

(1946) extended this study to a trial of urethane upon malignant disease in man. They found that in many cases there was a marked fall in the leucocyte count and therefore determined to test the drug in the treatment of leukemia. Of 32 cases of chronic leukemia the total white cell count fell dramatically in all but two, and in favourable cases the spleen and lymph nodes decreased in size and the haemoglobin level rose. These effects were only temporary as recurrences took place. The same workers gave urethane to 24 other patients with advanced malignant disease and in seven of these there was marked improvement including one case of lymphoepithelioma secondary in lymph nodes. Following the work of Paterson et al urethane was issued in many parts of the world in cases of malignancy including prostatic cancer (Huggins et al 1947), multiple myelomatosis (Harrington and Moloney 1950), the reticuloses (Melick 1952), nasopharyngeal carcinoma (Stock 1950) and the leukemias. Although urethane excited a palliative and not a curative action it was thought that there was a place for urethane in the treatment of cancer in view of the advanced and hopeless nature of many of the cases which responded.

Urethane was found to have various toxic effects



of which anorexia, nausea and vomiting were the most common. Leucopenia, agranulocytosis, hypoplastic anaemia, thrombocytopenia, liver damage and loss of weight in excess of that accounted for by low caloric intake were all observed. One case of primary carcinoma of the liver developing in a patient treated with urethane for myelogenous leukemia was reported. (Evans et al 1949).

#### Treatment of patients in the present series with urethane.

19 patients were treated with urethane. No fixed criteria was used for the selection of cases to be treated in this way. In the initial period of this study, patients were forced to wait for three or four months before commencing radiotherapy and urethane was given so that some form of treatment might be instituted at once. It was also given to patients who were considered too far advanced for X-Ray treatment. Latterly it was given to two patients who had failed to respond to radiotherapy.

#### Dosage and Administration.

Dosage was calculated by the method used by Haddow and Sexton in rats, 0.25 Gms. per Kilogram of body weight. In view of the severe toxic effects observed in the early cases it was later decided to

limit the dosage to a maximum of 12 Gms. This dosage was given daily for 6 days, but in several cases a day or more was allowed to elapse between doses because of systemic disturbances. Wherever possible a full course of 6 injections was given. The method of administration was that advocated by Stock, the urethane being given intravenously. An intravenous drip of 5% dextrose was set up, and allowed to run for a few minutes. The urethane, which was dissolved in a quantity of sterile water varying from 20-30 ccs. was then injected into the tube with the dextrose still running slowly. The drip was immediately allowed to flow rapidly for a few minutes and then continued at a slower but still fairly rapid rate until 2 pints of dextrose had been given.

#### Routine Investigations.

A complete blood count, a photograph, an X-Ray of the skull, a record of the body weight and biopsies of the nasopharyngeal and/or cervical lymph nodes were taken before treatment began. During treatment, a daily total and differential white count were done. Haemoglobin level and weight were estimated at frequent intervals. After treatment, further photographs and biopsies were taken wherever possible in all cases who had responded to therapy. Table XVII gives details and results of treatment in 19 cases.

TABLE XVII. URETHANE THERAPY

Case	Sex Age	Total Dosage in Gms	Number of Injections	Side effects	Lowest Total White Cell Count	Immediate Results	Progress	Other Treatment
1	F 32	31.5	3	Vomiting Haematemesis Giddiness	4,300	Discontinued	Died 6 months after treatment, 1 year from onset	T.E.M.
4	M 37	70.5	6	Drowsy Rigor	2,800	Improved. Cervical glands disappeared months after ure- thane, 17 months from onset		
5	M 52	70.5	6	None	8,000	No response	Unknown	
6	M 48	18	2	Rigor	8,600	Discontinued	Died 8 months after urethane, 44 months from onset	T.E.M.
7	M 32	32.25	3	-	6,000	No response	Deteriorated rapidly and died while under treatment	
8	M 45	23	2	Fell asleep Nausea Vomiting	4,700	Discontinued	Unknown	T.E.M.



TABLE XVII. Continued URETHANE THERAPY

Case	Sex Age	Total Dosage in Gms	Number of Injections	Side effects	Lowest Total White Cell Count	Immediate Results	Progress	Other Treatment
10	M 44	30	3	Disorientated Drowsy Nausea	6,500	Refused treatment	Unknown	
16	F 47	47.1	6	Giddiness Ataxia Vomiting	4,000	Improved. Became free of pain.	Died 11 months after urethane, 15 months from onset	
18	M 42	90	6	Drowsy, Giddy, Hysterical, Vomiting	4,000	Improved. Glands decreased markedly.	Recurred 1 month. Died 5 months after urethane, 11 months from onset	Radio- therapy
20	M 41	66	6	Drowsy, Rigor, Shivering	3,100	Improved. Cervical glands decreased in size markedly.	Recurred 4 months Alive	Palliative Radio- therapy
19	M 48	18	2	Rigor	8,600	Discontinued	Died 8 months after urethane, 44 months from onset	T.E.M.

TABLE XVII. Continued URETHANE THERAPY

Case	Sex Age	Total Dosage in Gms	Number of Injections	Side effects	Lowest Total White Cell Count	Immediate Results	Progress	Other Treatment
21	M 51	72	6	None	5,000	No response	Unknown	Radio- therapy
23	M 45	62.5	5	Dizzy	5,000	Improved. Primary smaller	Alive months after urethane, 26 months from onset	Radio- therapy
29	M 34	63	6	Nausea	3,400	Improved. Glands decreased slightly	Deteriorated rapidly presumed dead.	Radio- therapy before urethane with no results
35	M 36	33	6	None	5,000	No result	Died 8 months after urethane, 18 months from onset	
36	M 53	40	4	Copious vomiting	5,000	Refused treatment	Lived 9 months after urethane unknown since	

TABLE XVII Continued URETHANE THERAPY

Case	Sex Age	Total Dosage in Gms	Number of Injections	Side effects	Lowest Total White Cell Count	Immediate Results	Progress	Other Treatment
41	F 33	9.5	1	Giddiness Nystagmus	6,500	Discontinued	Alive 17 months after urethane, 23 months from onset	Radio-therapy
45	M 37	11	1	Rigor Vomiting	7,100	Discontinued	Alive 13 months after urethane, 37 months from onset	Radio-therapy
90	M 27	66	6	Fell asleep Vomiting	4,000	Improved, glands decreased slightly	Glands increased again immediately Alive	Previous Radio-therapy initial good result with recurrence which was radio-resistant



In all 10 patients were therefore able or willing to complete a full course of urethane. Case 23 had only 5 injections because X-Ray therapy began after the fifth, but he was given a total of 62.5 Gms. of urethane and is included among those who completed treatment. Of these 10, 7 patients improved a decrease in either the primary tumour or cervical lymph nodes or both taking place. In case 4 the glands have disappeared completely and it was not possible to remove one for histological examination after urethane. The improvement never lasted for more than 4 months.

Of the remaining 9 patients, two refused to complete treatment because of nausea or vomiting. The general condition of one patient was deteriorating so rapidly that treatment was discontinued and the patient died two days later, and in six patients it was not felt justifiable to continue with treatment because of the severity of the toxic effects. These severe effects were rigors in three patients, excessive vomiting in two of which one was bloodstained, and in one girl there was immediate rapid nystagmus after the first injection lasting 3 minutes and giddiness lasting for 5 days.

The side-effects may be briefly summarised.

Anorexia and nausea were complained of by 9 patients and in 7 this progressed to vomiting, and in one to haematemesis. In one case the leucocytes count fell below 3,000. There was no change in the differential white count. Four patients developed rigors, 2 with signs of an acute chest infection. The anaesthetic effect of urethane was demonstrated in 6 patients who became very drowsy while having the drug administered and in some cases fell into a deep sleep. One patient said it made him feel "drunk" and another after an initial period of drowsiness became hyperexcitable and required sedation.

It is interesting to note that of the 7 patients who responded to urethane, all had toxic symptoms and a leucocyte count of 5,000 or less. On the other hand the 3 who did not respond to treatment in spite of full dosage exhibited no side effects and the white cell count never fell below 5,000.

#### Progress

Of the 7 patients who improved with urethane, 3 are alive, 3 dead and one who attended regularly as an out-patient and whose condition was deteriorating rapidly is presumed dead as he failed to return. Of the patients in whom urethane had no effect or who could not tolerate the drug, 2 are

alive, five dead and the progress of five is unknown.

#### Additional Therapy

During urethane treatment a soft fluid diet and a plentiful supply of glucose drinks were given. In the case where the total white cell count fell below 3,000 pentose nucleotide (10 ccs. of 10% solution) was given daily for seven days by which time the leucocyte count had risen above 3,000.

One hundred milligrams of pyridoxine were given intramuscularly half an hour before urethane to lessen the severity of anorexia, nausea and vomiting.

Radiotherapy was given to six patients after urethane, and all responded to this form of treatment for a time at least. Two patients who failed to respond to X-Ray treatment were given urethane with temporary reduction in the size of the cervical lymph nodes.

Four patients who did not respond to urethane were given triethylene melamine later.

#### Pathology

Three of the cases who responded to urethane had biopsies carried out after treatment. Case 18 before urethane was histologically anaplastic carcinoma. The tumour was composed of solid masses of epithelial cells with ill-defined cytoplasm and large vesicular nuclei.



Mitosis was frequent. The stroma was vascular, scanty and contained lymphocytes and plasma cells. After urethane definite squamous areas could be seen with a few areas of prickle-cells but mainly composed of cells with dark staining nuclei. The stroma was more fibrous and more vascular.

Case 20 before urethane was histologically one of the intermediate group, consisting of masses of epithelial cells, some with vesicular nuclei, some with hyperchromatic nuclei and there were a few areas of Prickle cells. There was a fibrous stroma containing only a few lymphocytes and plasma cells. After urethane the epithelial masses were more compact and appeared on the whole better differentiated. The stroma was denser than before.

Case 29 was also an anaplastic carcinoma without lymphocytes. After urethane the appearance was more that of a transitional cell carcinoma, giving an impression of more differentiation than before. The stroma was again more fibrous and vascular.

### 3. Tri-ethylene Melamine (T.E.M.)

Triethylene melamine (2,4,6 triethyl-amino-S-triazine) a nitrogen mustard-like substance was originally used in the textile industry to improve

the finish of rayon fabrics. After the second world war its biologic effect on animal tissues was investigated when it was found to have a therapeutic effect in leukemia in mice (Burchenal et al). Thereafter a trial of T.E.M. in the treatment of leukemia and other malignant disease in man was instituted. It was observed to produce an improvement in chronic lymphetic and myelogenous leukemia, Hodgkin's disease, lymphosarcoma and mycosis fungoides (Bayrd et al, Wright et al).

Although the regression was of short duration in many cases in some it was maintained for a considerable period. Recently improvement in cases of ovarian cancer treated with T.E.M. has been reported (Sykes et al 1955).

Like urethane, T.E.M. produces symptoms and signs of toxicity. These fall into two groups (1) Immediate effects which consist of anorexia, vomiting and diarrhoea and (2) Delayed actions including leucopenia, renal damage, eosinophilia and hypoplasia of bone marrow. Transient haematuria, raised blood nitrogen and uremia have been reported (Karnofsky et al 1951, Mayer et al 1951).

Triethylene melamine was given to seven patients in this series. Four had previously been treated with

urethane without improvement. All were very advanced cases of nasopharyngeal carcinoma.

The dosage given was 2.5 mgms. of T.E.M. daily for 4 days. This was taken by mouth with a glass of water on waking in the morning one hour before breakfast. In case 8 this dosage was given for 6 days making a total of 15 mgms. One case (Case 8) with a metastasis in the sternum showed diminution of this deposit, but the improvement lasted only one month. The total cell count fell to 1,600 after ten days and remained between 1,000 and 2,000 for 3 weeks in spite of pentose nucleotide injections. The polymorphonuclear cells were affected more than the others. In the other six patients no improvement took place. Four patients are dead and the progress of the other three is unknown.

#### 4. Surgery

The use of surgery was limited to taking a biopsy for histological diagnosis in the vast number of cases. In 3 patients who had intractable pain, beyond relief by drugs or by radiotherapy a bilateral prefrontal leucotomy was performed by Professor Mekié. Two patients were relieved of their pain, but one became unmanageable and had to be transferred to a mental



hospital, and the third died following operation. Two patients with spinal metastases who developed retention of urine required suprapubic cystotomy.

One patient with severe keratitis had a tarsorraphy performed.

## 5. Radiotherapy

This form of treatment was the only one which was felt to hold out any hope of cure of the disease. In many cases due to the advanced nature of the disease even this could only aim at palliation. The patients were therefore placed in two categories.

1. Those in whom there was no evidence either on clinical or radiological investigation of intracranial extension, or of distant spread of the disease and in whom the effect of irradiation could hope to be radical. Ideally patients who exhibited on examination only a nasopharyngeal tumour with no lymph node metastases were the candidates for radical therapy but only two such cases were seen.

Cervical lymphadenopathy whatever its magnitude was not, however, considered a hopeless sign in treating the disease.

2. Those in whom there was evidence of invasion of the skull in whom only palliative treatment could be

given. Apart from the technical difficulties of irradiating the nasopharynx treatment of the patients in Singapore presents other problems. They tolerate the discomforts due to radiotherapy badly and are all too liable to refuse further treatment if skin reactions or local reactions causing sore throat, and dysphagia occur. Conversely if they feel well in themselves they seem unable to appreciate the necessity for completing a course of therapy, however blackly the ultimate prognosis may be painted to them if they stop treatment. The author is indebted to Dr. J. K. Ritchie of the Radiotherapy Department, Civil General Hospital, Singapore for the technical details of radiotherapy given to the patients in this study.

Treatment by radiotherapy in these cases was confined to the use of X-Rays and neither radium nor radioactive cobalt sources locally in the nasopharynx were employed. All patients were treated either at 250 K.V. with a half value layer of 3.7 mms. cu. or at 400 K.V. with a half value layer of 3.8 mms. cu. the resultant depth doses being almost identical.

Palliative Treatment consisted of treating two large lateral fields extending from the base of the skull to the clavicle, and measuring 21 x 28 cms. The daily input rate on these large fields was usually

250 r to one field, and the total dosage given to these fields was 3,000 r skin dose to each side, over a period of four to five weeks. This resulted in an approximate depth dose to the nasopharynx of 4,500 r. Standard depth doses were used throughout and no allowance was made for bone absorption.

Radical Treatment consisted of the use of two lateral fields as above with the addition of two small lateral fields to the nasopharynx of 5 x 5 cms. or oblique fields of 6 x 6 cms. An attempt was made to give a dosage of 6,000 r to the nasopharynx over a period of about six weeks.

Retreatment was given for the following causes.

(a) Progressive cranial nerve lesions, particularly where there was increasing deterioration of vision

(b) Progressive erosion of the base of the skull radiologically

(c) Progressive and unbearable headache.

In these cases (a) (b) and (c) irradiation was directed at the base of the skull. X-Rays generated at 250 or 400 K.V. with heavy filtration were used in an attempt to avoid increased absorption in unaffected bone through which X-Rays must pass before reaching central or paracentral area of the skull

(d) Retreatment to the primary nasopharyngeal



tumour or to cervical lymph nodes if there was a recurrence in either situation.

Treatment of skeletal metastases was instituted as soon as these were diagnosed. In general these deposits were less radiosensitive than the corresponding primary tumour or the lymph node metastases.

Local and systemic effects of irradiation.

In general systemic disturbances among the Chinese patients are rare. Anorexia is common but nausea and vomiting rare. General fatigue towards the end of treatment was almost constant but in few cases did the patient require hospitalisation. As previously mentioned the most difficult problem was that of persuading the patient that these were only a result of treatment and would pass off after this was completed. Routine blood counts showed little upset.

The local effects were severe. Chinese skin tolerates a high dose of irradiation before proceeding to moist desquamation but skin reactions were frequently augmented by scratching and no amount of explanation could prevent this occurring. Soreness of the mouth and pharynx and dysphagia were severe but were relieved by local and general analgesics. An emulsion containing aspirin was the most soothing remedy. The

provision of suitable diet also became a problem but patients were usually able to take their rice in soup and the diet was supplemented by heavy protein feeding with caseinhydrolysate. Iron and vitamins were given throughout treatment. Effects on the larynx were slight but a temporary loss of voice did occur in some patients.

#### The Results of Radiotherapy.

In all 90 (80.4%) patients were treated with X-Rays. Of these 27 fulfilled the criteria for radical treatment, i.e. there was only a puniary nasopharyngeal tumour and/or enlargement of the cervical lymph nodes, and there was no neurological or radiological evidence of extension of the disease to the skull. Therefore in 70% of patients treated with X-Rays, the treatment could only be palliative from the beginning.

Table XVIII summarises the results of treatment in both those treated radically and palliatively. Of those treated radically, three refused to complete treatment and three were still under treatment when the survey ended. Of those treated palliatively ten refused treatment, two were still on radiotherapy and three had distant metastases when they were first treated.

TABLE XVIII RESULTS OF RADIOTHERAPY

	Total	Initial good result	Recurrence of glands	Recurrence of Primary	Development of cranial nerve lesions	Development of distant metastases	Alive without Symptoms	Alive with Disease	Dead	Unknown
Treated Radically	21	20	3	-	3	3	10	4	2	5
Treated Palliatively	44	38	5	1	10	15	4	19	8	13



An initial good response denotes disappearance of the nasopharyngeal tumour and of the cervical lymphadenopathy. One case in the radically treated group showed no diminution in the size of either, as did one of the palliatively treated group. In this second group 5 other patients failed to respond satisfactorily, in three only a very slight diminution occurring, in one the glands disappeared but the primary persisted and in another the primary appeared cured but the glands showed no response. The histology of these cases which failed to respond were 1 differentiated squamous epithelioma, two lymphoepitheliomas, three undifferentiated squamous epithelioma and one anaplastic carcinoma.

Recurrence of Glands was treated but the response was never so good as it had been initially and in two cases there was no diminution in size whatever. Similarly when the recurrent nasopharyngeal tumour was treated, or an initially radioresistant growth was retreated the response was poor. Histologically all the tumours or their lymph node metastases which recurred belonged to the intermediate group.

Cranial nerve lesions developed de novo in the first group after treatment, in the case of the second group this denotes involvement of further cranial

nerves. Abducens paralysis trigeminal neuralgia and ptosis all recovered in one or two cases after radiotherapy. In no case was there any appreciable regrowth of the bones of the skull when seen radiologically.

The incidence of distant metastases was much higher in the second group than in the first but this is understandable when one considers that the disease was more advanced in the second group.

Follow-up. Nearly 50% of the first group were alive and with no evidence of the disease after an average of 7.4 months following treatment. The longest duration since treatment was eighteen months. Of the patients treated palliatively there were only four (9.1%) alive and symptom free after an average interval of 15 months after treatment. As erosion of the skull persisted these cases could not be definitely considered as free from disease. Four (19%) of the first group and 19 (43.2%) of the second group were alive but with definite evidence of disease. Many of these were given retreatment to the base of the skull or to metastases. The benefit of palliative treatment in those with marked visual disturbances was marked, and appeared to be maintained for several months. The response of distant metastases to

radiotherapy was disappointing. Two of the first group and eight of the second group died, within 10 months or 7 months on the average respectively. Of the others listed as unknown, two of the first group and six of the second group are presumed dead as they had attended regularly as outpatients and were all deteriorating many with distant metastases and multiple cranial nerve lesions, and simply failed to return.

In all therefore out of 90 patients who were given radiotherapy, only 10 can be said to be free of disease. The length of time since these patients were treated is too short to allow any assessment of five year survivals. There is however at the present time only one patient attending the Radiotherapy Department who has remained free of symptoms for five years.

#### FOLLOW-UP

As far as possible patients returned to the follow-up out-patient clinic at weekly or fortnightly intervals. Many patients attended faithfully and a sudden failure to return in any case where the disease had been advancing steadily was highly suggestive of death. Where patients failed to return attempts were made to contact them or their relatives in order to ascertain the reason. Unfortunately few letters evoked any response, and many were



returned unopened. Visits were made to houses in some cases but numbering of houses in Singapore is disorganised in the extreme and finding them is a time-consuming task. The patients who lived off Singapore Island were even more difficult to trace. Most had no medical attendant who could supply news of progress.

Table XIX shows the follow-up records of all 112 patients, by whatever method treated.

TABLE XIX

Progress

	Total	%
Alive	44	39.3
Dead	24	21.4
Presumed dead	20	17.9
Unknown	24	21.4
TOTAL	112	100

Those who were alive had lived for an average of 22 months since the onset of disease. The longest survival was 69 months (Case 58). This man had had glands of the neck removed three times before he was correctly diagnosed and referred to Singapore. He had a primary nasopharyngeal tumour, bilateral enlargement of the glands in the neck, multiple cranial

nerve lesions and invasion of the skull. He was treated with radiotherapy after which the glands and primary disappeared but the cranial nerve lesions persisted. He was alive 9 months after treatment, having a five year history when he presented. Only ten of the patients who were alive could be said to be free of disease.

Of those who had died, the average duration from the earliest symptom to death was 22.5 months, the longest life being 59 months (Case 49). This was a Chinese schoolboy of 17 years. He had a four year history of epistaxis, for which three nasal operations had been performed, and three biopsies taken from the nose, all negative. He had a tumour in his nasopharynx, bilateral cervical lymphadenopathy and erosion of the middle cranial fossa. He was treated with radiotherapy with complete disappearance of glands and primary. Eleven months later he returned with severe pain in his dorsi-lumbar spine. Radiologically there was erosion of the ala of the sacrum. He rapidly became paraplegic, developed retention of urine and faeces, and died within a month in spite of palliative radiotherapy.

## DISCUSSION

Nasopharyngeal carcinoma with its numerous aspects provides a subject for discussion which could continue almost indefinitely. It is a subject which cannot fail to intrigue anybody who has experience of it whether he be otolaryngologist, neurologist, radiologist, pathologist or general practitioner. The radiotherapist is perhaps more perplexed than intrigued by the problem and in the realm of treatment one hopes that future developments may provide a more satisfactory outcome of therapy than can be achieved by present day methods. While this discussion will deal largely with the pathology of nasopharyngeal carcinoma, other aspects of the disease must first be considered.

The clinical features of nasopharyngeal carcinoma are similarly described by most writers on the subject. Many series of cases are small and while they may include some interesting feature of the disease cannot be relied upon to give a significant indication of the frequency of any one symptom or sign. Digby, Godtfredsen and Simmons and Ariel all described a large number of cases.

All authors are in agreement that the clinical features fall into the following groups:-



1. Enlargement of the cervical lymph nodes
2. Nasopharyngeal symptoms and signs
3. Auricular symptoms and signs
4. Cranial nerve lesions and radiological changes in the skull.

That cervical adenopathy is a common and early feature of the disease is stressed by most authors. In the patients seen in the present series, it was the commonest early symptom and the most common finding on examination. Although frequently bilateral one side was commonly involved before the other and Digby's description of asynchronous and asymmetric enlargement of lymph nodes was borne out by the findings in this study.

The nasopharyngeal symptoms and signs while they may be absent, as New pointed out, are not rare. Symptoms of epistaxis, nasal obstruction and anosmia or all, occurred in 75% of patients in this series and on the average appeared 6 months after the onset of disease. In 24.1% of patients they constituted the initial symptom.

A tumour was found in the nasopharynx of 89.3% of patients and was absent in only 12 patients. It does seem therefore that careful examination of the nasopharynx and an awareness of the disease will reveal

the presence of a primary tumour in most cases of nasopharyngeal carcinoma. The two macroscopic types of growth correspond to the description given as long ago as 1911 by Trotter who noted one which projected into the cavity of the nasopharynx and one which did not. The infiltrative nature of these tumours under the mucosa through the surrounding tissues and along and through the base of the skull is well shown by clinical, radiological, histological and post mortem examination.

The ear symptoms of deafness and tinnitus are due to obstruction of the eustachian tube, either by tumour or by catarrhal changes secondary to the neoplastic process occurring near its orifice. Of Digby's 210 cases none had an eighth nerve lesion and this was not seen in any case of this series. Roger et al, and Flynn have described cases where all twelve nerves of one side were involved, Ball described a patient with a non-functioning labyrinth due to tumour at the internal auditory meatus and Ballenger recorded a case where the auditory canal was filled with tumour. Involvement of the eighth nerve may therefore occur but it is the exception and certainly not the rule.

Furstenberg described changes in the tympanic membrane secondary to circulatory disturbances in the



middle ear and these changes were seen in 10 cases of this series. A chronic discharge from the middle ear may also occur due to circulatory or inflammatory disturbances secondary to eustachian blockage. Fox described a patient with tumour in the middle ear but was unable to decide if it had come through the eustachian tube or the petrosa. The former would seem more probable providing a space for easy expansion of tumour whereas lateral extension through the petrous temporal which is the thickest bone in the body, would imply extensive erosion by tumour.

The literature about the cranial nerve lesions in nasopharyngeal carcinoma is perhaps less straightforward. The numerous syndromes which have been used to describe various combinations of nerve lesions tend rather to obscure than to simplify the subject. From the diagnostic standpoint the most helpful contribution is that of Jefferson who considers that unilateral nerve palsies or inconsequent palsies of several cranial nerves are strongly suspicious of nasopharyngeal tumour.

Godtfredsen was the first writer to stress that neurological symptoms might be an early sign of disease. In this series the initial symptom was referable to the cranial nerves in 9.8% of cases. On the average symptoms appeared 8.6 months after the onset of disease



and patients did not on the whole come till the history was of 12.8 months duration. 59% of patients had cranial nerve symptoms when they presented at hospital, and 71 (63.4%) patients had cranial nerve lesions altogether. Follow-up of patients showed the appearance of further cranial nerve lesions as the disease progressed.

The incidence of neurological lesions in this series is therefore much higher than that quoted by Godtfredsen (38%) or Simmons and Ariel (36.6%). A previous analysis of the cranial nerve lesions by the present writer (Lawley 1955 b) showed an incidence of 48% cranial nerve lesions in 185 cases. Many of these patients were seen before the present study was begun, the information being collected from case records and no follow-up examination was carried out. It would appear that the incidence of neurological involvement is even commoner than has been appreciated.

Trigeminal neuralgia or numbness was the earliest neurological symptom commonly in the second division of the nerve, and trigeminal lesions were the commonest finding. Visual disturbances did not occur till about the time that the patient presented at hospital. This was no coincidence as failing vision appeared to incite even the stoical Chinese to seek medical attention.

The abducens nerve was also frequently involved.

These findings agree with those of other writers. Woltman quotes VI followed by V, Needles VI and V, Godtfredsen V and VI, Simmons and Ariel VI, XII and V as the most common cranial nerves affected. Jefferson says that symptoms of invasion of the cavernous sinus and trigeminal nerve are the first sign of nasopharyngeal malignancy in one third of cases. He thinks that spread occurs through the foramen lacerum to involve the trigeminal ganglion and the nerves of the cavernous sinus. Godtfredsen agrees with this view but suggests an alternative method of spread to the parapharyngeal space to involve the nerves in the jugular foramen and hypoglossal canal. Woltman thought the nerves were involved extracranially most often while Schlivek considered that they were always involved at the nasal foramina. Williams postulated that tumour could spread through the foramen lacerum by soft tissue continuity without involving bone.

One must consider the evidence which is provided by this present study and by a study of the anatomy of the region. 62.6% of tumours arose in the lateral wall in the region of the eustachian tube and of the fossa of Rosenmüller. The latter lies directly under the foramen lacerum which is bordered

by the trigeminal ganglion and which lies in close relation to the cavernous sinus. The nerves first met in approaching the sinus are the maxillary nerve and the abducens nerve. Other nerves of the sinus and the optic nerve were never involved without concomitant lesions of the maxillary or sixth nerves. Invasion of the sphenoid sinus by tumour is common and this is separated from the cavernous sinus only by thin bone. Erosion of the middle cranial fossa, commonly in the region of the petrous apex was present in 81.2% of cases.

77.4% of tumours of the lateral wall, 86.6% of tumours of the roof and 50% of tumours of the posterior wall produced clinical or radiological evidence of intracranial invasion.

Tumours of the vault however only constituted a small group (15.2%) of all lesions. Spread occurs either (1) through the foramen lacerum to involve the trigeminal nerve, the nerves of the cavernous sinus and may continue forward to involve the optic nerve, this being the common method of extension of tumours arising from the lateral wall or (2) through the sphenoid sinus to the cavernous sinus in the case of tumours of the vault.

The third division of V may be involved by lateral



extension of tumour from the nasopharynx, or when it is involved with other branches of V at the trigeminal ganglion. It was only involved with the motor division without other branches of V in two cases so that involvement at the foramen ovale cannot be common.

The motor division of V lies under the trigeminal ganglion and is probably involved there by spread through the foramen lacerum.

Godtfredsen considers that exophthalmos may arise either from spread to the superior orbital fissure forward from the cavernous sinus or to intraorbital fissure via the parapharyngeal space. In the six cases of exophthalmos seen in this series there was massive erosion of the skull, and it would seem that Godtfredsen's theory is correct.

The last four cranial nerves may be involved at their exit from the skull by extension of tumour along the base, by glandular metastases in the neck, or by steady lateral infiltration of tumour to the parapharyngeal and retroparotid spaces. Of the ten cases in which one or more of these nerves was involved without an accompanying lesion of any of the higher cranial nerves only one showed erosion of the skull, but overall 59.6% of lesions of the ninth to twelfth cranial nerves showed destructive changes in the

cranium. Glandular metastases need not be massive to involve these nerves as the first evidence of lymph node involvement appears opposite the external jugular vein and near the exit of these nerves from the skull. The high incidence of vagus lesions is accounted for by palatal paresis and by dysphagia due to paralysis of the superior constrictor muscle. In many cases these pharyngeal branches must be involved by direct extension of tumour. The laryngeal branches were affected only when there was gross adenopathy and are probably paralysed by direct pressure of glands. Where the eleventh nerve was injured alone this was probably due to pressure by lymph node metastases. The seventh nerve is involved at the stylomastoid foramen. If it were affected at the internal auditory meatus one would expect an associated lesion of VIII which does not occur. That cranial nerves may be involved by pressure rather than infiltration is demonstrated by recovery of their lesions after radiotherapy.

The nerve of the pterygoid canal was only affected once in this series. Digby describes a woman who when she cried shed tears only from one eye, no doubt due to a lesion of this nerve. Flatman considers that lesions of this nerve are rare only

because they are not suspected but it does not seem that they are so frequent as he suggests. The average age of this series corresponds to that given by other writers although Digby found it to be slightly lower i.e. 35 - 39 in males, 30 - 34 in females. The preponderance of males over females agrees also with the findings of other writers.

Aetiology. The high incidence of nasopharyngeal carcinoma among the chinese has been noted by many. Thomson's description of 'cervical lymphosarcoma' includes the interesting statement that many of these patients had nasal obstruction. No doubt the glandular enlargement was secondary to a nasopharyngeal neoplasm. Bercovitz's contention that the disease is common in Hainan, less so in Canton and Hong Kong and less frequent still north of these places is interesting in view of the relatively high proportion of Hainanese and Cantonese in this series. Wang who had seen only 36 cases of nasopharyngeal carcinoma in 6½ years writes from Chengtu, 900 miles north of Hainan. Hara described the higher incidence in people from Southern China than from the North and concluded that this denoted a hereditary influence. Bonne speaks of the high incidence of cancer of the neck glands in people of the Far East and his description of "reticuloendo-



thelioma" corresponds to the histological appearance called lymphoepithelioma by other writers. Martin and Quan, and McNaught report a large proportion of cases of nasopharyngeal carcinoma among Chinese living in the Americas, the latter finding it 20 times more common among his Chinese patients than among the rest of the population of San Francisco. Digby describes nasopharyngeal carcinoma as the second most common form of cancer in Hong Kong, accounting for 18% of all forms of malignant disease and Mekie cites it as the third most common cancer in Singapore where it comprised 16.41% of all malignant neoplasms. In this series 100% of patients living in Singapore were Chinese although the proportion of Chinese in the general population is only 76.5%. Comparison with figures from America, 0.7% of all cases of cancer (Simmons and Ariel), from Scandinavia 0.4% of all malignant disease (Godtfredsen), from England 6 in 1 million (Lambert) and from India 1.85% of cancers (Das et al) is dramatic.

The evidence for a high incidence of nasopharyngeal carcinoma among the Chinese is overwhelming. As it occurs among Chinese out of China it is reasonable to suppose that hereditary influences play a part. What the exciting factor may be is more difficult to

determine. Dobson's theory of a smoke-laden atmosphere seems feasible but Martin and Quan have pointed out that the incidence of nasopharyngeal carcinoma is high among Chinese living in good conditions. The writer has often heard Dr. Ballasingham of Singapore, whom Digby quotes, teaching the medical students that opium smoking is the cause of the disease. Only one of the present series was an opium addict. There does not seem to be any evidence to support this statement. The eating of hot food, hawking of phlegm and the theory of intracellular viruses in the causation of nasopharyngeal malignancy have been discussed and discounted by Digby. The burning of joss-sticks is peculiar to the Chinese and constant inhalation of their vapour might be an aetiological factor in the production of the disease among Chinese. An effort was made to analyse joss-sticks and their vapour chemically but unfortunately the chemists could not spare the time to carry out this work. It may be that joss-sticks contain some carcinogenic substance.

#### Differential Diagnosis.

The numerous times in which misdiagnosis was made in cases of nasopharyngeal malignancy was stressed by New in 1921. Since then the disease has been described in medical journals all over the world. In

centres such as Singapore and Hong Kong where it is common the medical profession are on the outlook for the disease and most cases are referred to hospital as soon as they consult their general practitioner.

Unfortunately the poorer-class Chinese usually wait to consult a doctor until a full-fledged clinical picture has developed and there can be no doubt of the diagnosis.

Difficulty arises mainly in the early stages where only one symptom or sign is present. Enlargement of the cervical glands is commonly thought to be due to Tuberculous Adenitis and in Singapore tuberculosis is prevalent. In several cases of nasopharyngeal carcinoma tubercle follicles have been seen histologically in the neck glands as well as carcinoma. Clinical or radiological evidence of Pulmonary Tuberculosis does not exclude the possibility of nasopharyngeal carcinoma, being present in a fair proportion of cases. Too often the disease is only diagnosed after the patient has been treated with streptomycin and P.A.S. and failed to respond. Clinical examination of the glands does not always settle the diagnoses. Examination of the nasopharynx may do so but a biopsy and histological examination is necessary to confirm or exclude carcinoma.



Hodgkin's disease, lymphosarcoma and leukemia may be considered when cervical adenopathy is the only finding. Examination of the blood and histological study of the glands will settle the diagnosis.

Where nasopharyngeal symptoms and signs prevail as the only feature of the disease, adenoids, nasopharyngeal fibroma in young people and nasal polypi in older people may be their cause. These must be excluded by clinical and histological examination.

Where a cranial nerve lesion develops, initially the diagnosis may well be missed. Trigeminal neuralgia may be diagnosed, and its cause not ascertained. One patient was thought to have an acoustic neuroma. Mandibular avulsion for severe pain in the distribution of the third division of V was performed in one patient in Sarawak without any idea of its cause. The existence of a tumour may be recognised but thought to be primary in the gasserian ganglion. Examination of the nasopharynx with biopsy and radiographs of the skull should reveal the diagnosis.

Where no tumour is present in the nasopharynx the problem is more difficult. In 12 cases of this series this feature was never present at any stage of the disease. Granted it might have appeared if radiotherapy had not been instituted, but by that time the

disease might well have been too advanced for treatment. Carcinoma may be diagnosed after biopsy of the neck glands but the primary not be detected. Of these 12 patients, a positive biopsy was obtained from the nasopharynx in one. Eight had symptoms of epistaxis, nasal obstruction and in 4 this was combined with deafness or tinnitus. Seven had erosion of the middle cranial fossa and two invasion of the sphenoid sinus on X-Ray. A thickening of the posterior nasopharyngeal wall seen radiologically was the clue to the location of the primary in one case.

Where there is a fully fledged picture of nasopharyngeal tumour, enlarged neck glands and cranial nerve lesions the diagnosis rests between carcinoma and other malignant tumours of the nasopharynx and this is a pathological problem. Lymphosarcoma is the most likely alternative diagnosis; this occurs younger and there may be widespread lymphatic enlargement. The pathological differentiation will be discussed later. Other malignant tumours which were not met with in this series but have been described include mucous gland tumour, angioendothelial sarcoma, malignant lymphoma, malignant chordoma, plasmacytoma, lymphoblastoma, craniopharyngioma, rhabdomyoma, myxosarcoma, osteosarcoma, alveolar sarcoma, round cell sarcoma,

salivary gland adenocarcinoma (Dichl) embryonic sarcoma and giant cell sarcoma.

### Treatment

Nineteen cases with nasopharyngeal carcinoma were treated by the writer with urethane. Previously twelve patients had been treated by this method in the Civil General Hospital, Singapore and of these six had improved. Seven of the present series showed a decrease in the cervical lymph nodes or the primary tumour or both. Stock has already pointed out that the disease does not regress spontaneously and the rapidity with which glandular enlargement shrinks is dramatic in many cases. Unfortunately it is a short-lived improvement, the longest period being four months after treatment. It did not in any way prevent the advancement of disease or prolong the life of the patient.

The toxic effects of urethane present a definite drawback to treatment. Nearly half the patients in this series were unable or unwilling to tolerate the drug. The toxic symptoms in those who completed urethane therapy were much more marked in those who improved than in those who did not. The therapeutic and toxic doses of the drug appear to approximate very



closely to each other. No fatal effects of the drug were noticed in this series but in one of the previous twelve patients treated, acute liver failure followed by death resulted and this was thought to be a direct effect of urethane.

The histological study of tumours which have responded to urethane is interesting in view of the work of Haddow and Sexton. They thought that after urethane there was an attempted differentiation on the part of the tumour cells themselves, and that this appearance was not merely secondary to changes in the stroma. In the cases studied here (and in four of the previously treated cases) a similar attempted differentiation on the part of the malignant cells did appear to take place after urethane.

Treatment by urethane is of value where the patient has to wait some time before receiving radiotherapy. If the primary tumour and cervical lymph nodes can be held in abeyance until irradiation begins the prognosis may be improved.

Where the disease is too far advanced for radiotherapy there does not seem much indication for urethane as its effect is only temporary and its side effects so unpleasant.

In cases of radioresistant carcinoma, urethane

may produce a temporary improvement which will encourage the patient. Triethylene Melamine does not appear to play any part in the treatment of nasopharyngeal malignancy. In the present state of our knowledge Radiotherapy is the only form of treatment which can hope to effect a cure. Varying five-year cure rates have been quoted by different writers, the best being that of Martin (1945) who had 50% cure rate in cases who had no palpable lymph nodes. When an overall figure is taken for all cases this is lower thus Kramer quotes 25.8% five-year cure rate and Lambert 30%. Kramer found that the best results were achieved with lymphoepithelioma and undifferentiated carcinoma and the worst with transitional cell carcinoma. Snelling considers that intermediate tumours which neither tend to be radioresistant or to metastasise before treatment can be completed.

It is not proposed to discuss the merits of the various radiotherapeutic techniques which have been described. The present consensus of opinion is that the neck glands should be treated by large field irradiation with X-Rays and the nasopharynx treated locally with X-Rays, radium or radioactive cobalt. Wilson's fenestration operation which provides a permanent opening into the nasopharynx for diagnostic

and therapeutic purposes is a decided advance in the treatment of the disease. The exploration of the base of the skull which he is at present carrying out through the fenestrum may open up new methods of treatment.

In view of the dramatic response evoked by urethane in some cases one feels that some other chemotherapeutic agent may be found which will effect a permanent cure.

#### The Spread of Nasopharyngeal Carcinoma

The primary nasopharyngeal tumour may spread

1. Directly (a) by infiltration under the mucosa
  - (b) upwards to the base of the skull
  - (c) laterally to involve muscles and nerves in the region
  - (d) posteriorly through fascia and prevertebral muscles to involve upper cervical vertebrae or through the occipito atlantoid ligament and thus into the cranium extradurally to involve cranial nerves.
  - (e) forward through the choanae into the nose
  - (f) downwards to depress the soft palate, or to project into the oropharynx.

Spread to the base of the skull has already been discussed. While cranial nerves are usually affected



extradurally, actual penetration of the dura mater was seen in post mortems carried out in this series and by other writers.

2. Via the lymphatic pathway to

(a) the regional lymph nodes. The constancy with which the glands opposite the external jugular vein and then gradually other members of the upper deep cervical group in the anterior triangle and later the glands in the posterior triangle denotes spread by permeation of lymphatics.

(b) to the supraclavicular and axillary lymph nodes. In all but one case where this was present there was gross lymphatic enlargement of the cervical glands. A post mortem report (of a patient who died before this study commenced) describes involvement of all the lymphatics from cervical to axillary lymph nodes. This would also appear to be due to permeation.

(c) to distant lymph nodes, e.g. in the mediastinum. This may occur by permeation, embolism or from deposits in the lung.

3. By the blood stream to the viscera and skeleton. Batson has described a system of vertebral veins which comprises veins of skull, brain, neck viscera, vertebral column and body wall and which constitutes a separate system from the caval, portal and pulmonary

systems. In this system of valveless veins retrograde spread is possible and he attributes many 'paradoxical' metastases to spread within this system. The longitudinal vertebral veins have many rich communications with veins in the spinal canal round the spinal column and within the bones of the vertebral column. It seems likely that the spread of nasopharyngeal tumours to vertebral column, sacrum and ilia, as well as to the cranial vault may take place via the vertebral system of veins.

#### Pathology

The difficulty of pathological diagnosis of malignant tumours of the nasopharynx is apparent when one studies the divergent terminology used by different experienced pathologists to describe these neoplasms. Willis (1954b) has emphasised that the only permissible method of classifying tumours is on histological grounds, together with division into innocent and malignant growths, and condemns methods founded on an embryological, aetiological or regional basis. The grading of tumours is always open to criticism and signifies rather an attempt to clarify description than a rigid division into separate groups. In the present series the tumours have been graded histologically

but the weakness of division into separate groups was encountered both because of the evident continuity of one pathological process throughout all three groups, and because of the variable histological appearances which might be found in different areas of one tumour.

The Group I lesions provide no special problem. They form a small group of definite acanthoma arising from the lateral nasopharyngeal wall. Two were small ulcers and in the third no lesion could be found in the nasopharynx. They lacked cornification, a fact easily explained on examination of the normal squamous epithelium lining the nasopharynx which does not cornify.

Here it is of moment to consider the exact nature of the squamous epithelium lining the nasopharynx in its postero-inferior part. It is a type of squamous epithelium which does not keratinise and presents a regular flattened appearance with little papillary formation. It does in fact lack the scaliness to which squamous epithelium owes its name. It is endodermal in origin as compared to epidermis or the epithelium of the oral cavity which are derived from ectoderm. Willis<sup>(1954c)</sup> has said that "the germ layers, the status of which has of recent years decreased greatly even for the embryologist are devoid of significance



for the pathologist". He further quotes Ewing who wrote "the behaviour of tumour cells is very much more influenced by the acquired characters of the cells of origin than by their embryological derivation". The fact that squamous cell carcinoma of the oesophagus which also arises from endoderm often shows marked cornification, suggests that the histological character of nasopharyngeal carcinoma cannot be explained by its embryological derivation. The stratified epithelium of the nasopharynx is directly continuous above and anteriorly with the ciliated columnar epithelium lining the nasopharynx and nasal cavities. While arising from the same source and being directly continuous with the epithelium of the alimentary tract, the stratified epithelium is in fact acting as respiratory epithelium. It is therefore a form of squamous epithelium modified both in its structure and in its function and it seems reasonable to accept that it can produce neoplasms peculiar to itself. While the term squamous is retained therefore to describe both the epithelium and the tumours arising from it, it must be remembered that it is not fully differentiated squamous epithelium.

The Group II lesions comprise 68.5% of the whole series. In this are included all undifferentiated squamous epitheliomata and the so-called transitional

cell carcinomata. It has been mentioned that in most cases the malignant process appeared to arise in the deeper layers of the epithelium. When these tumours arise from the lateral or posterior walls as they did in 63.8% and 18.8% of cases respectively, it seems reasonable to regard them as neoplasms arising from the deeper layers of an undifferentiated form of squamous epithelium. In 17.4% of cases however growths which arose from the nasopharyngeal vault were found to fall into the intermediate group. Where these tumours revealed squamous characters, a careful study of the epithelium from which they arose revealed that squamous metaplasia took place in the deepest part of the lining columnar epithelium. Moreover their lymph node metastases presented an appearance identical with those of the squamous epitheliomata.

The transitional cell carcinomata were in many cases indistinguishable from non-cornifying squamous epithelioma. Ewing has observed how much the structure of nasopharyngeal tumours may vary in different areas and this was a frequent feature of the tumours studied here. Many tumours whose origin could be traced from lining squamous epithelium were composed of solid columns of cells with scanty cytoplasm and dark-staining nuclei, reduplicating



exactly the appearance of transitional cell carcinoma. This histological picture was also given by some tumours which arose from the basal cells of the columnar epithelium. Kramer has described transitional cell carcinoma as originating in the columnar epithelium whereas Quick and Cutler and Ewing have cited the lining cells of the schneiderian membrane or the cells at the base of the nasopharyngeal crypts and sinuses as a possible origin of this tumour. That a modified type of epithelium similar to the transitional epithelium lining parts of the urinary tract may occur in the deeper parts of the nasopharynx such as the base of the crypto is undisputed but it does not seem justifiable to regard it as a separate entity from the stratified epithelium lining the more superficial parts of the nasopharynx. The main point which has differentiated transitional cell carcinoma of the nasopharynx from squamous epithelioma has been its greater radiosensitivity. This is a property of all undifferentiated tumours and does not justify the introduction of a special class of neoplasm.

Quick and Cutler offered an alternative explanation of the origin of transitional cell carcinoma namely squamous epithelium which had lost its adult character. From a study of the tumours in this



section it does seem that they are indeed poorly differentiated squamous epitheliomata arising in the squamous epithelium or as the result of squamous metaplasia in the ciliated columnar epithelium of the nasopharynx.

The Group III lesions comprise 28.8% of all tumours. They present two main problems. Firstly, are they indeed carcinoma and not sarcoma, and secondly does lymphoepithelioma constitute a separate class of neoplasm from the remainder of the group?

The vast majority of these carcinomata present histologically as solid masses of tumour cells arranged in an alveolar pattern which is accentuated by reticulin staining. Lumb and Willis (1954 d) among others have emphasised that where a tumour is of such a degree of anaplasia as to make it impossible to classify it as carcinoma or sarcoma by other methods, the relation of the reticulin fibres to the tumour cells is not sufficient evidence on which to base a diagnosis. However these tumours did present the alveolar architecture of a carcinoma and even in the most anaplastic tumours careful search revealed a few areas of definite malignant epithelial cells. Further the effect of urethane upon anaplastic carcinoma was to make it present definite epidermoid

characters. A sarcoma does not become epithelial whatever treatment is given.

Three cases were seen over the same period as the 112 in this series which appeared sarcomatous histologically, and which presented clinically as lymphosarcoma. All the tumours in this series were acceptable microscopically as carcinoma.

Lymphoepithelioma as originally described by Regaud and Schmincke possessed two main characters (a) its high radiosensitivity and (b) the admixture of epithelial cells and lymphocytes. As has previously been pointed out radiosensitivity is not peculiar to any one tumour. Lymphoepithelioma only occurs in those regions where epithelial cells and lymphocytes normally exist in close relation to each other, i.e. in the lymphoepithelial organs of Jolly and Mollier. Examination of the tumours of those regions where epithelial cells and lymphocytes are still closely related demonstrates why Jovin thought that the epithelial cells exerted a chemiotaxic effect upon the lymphocytes. His evidence was based largely on one post mortem report by Derigs where lymphocytes were found lying among the epithelial cells in bone, lung and liver metastases. Inspection of the photomicrograph of a lung metastasis in Derig's paper



does not convince one that his conclusions are justified. The epithelial cells are very anaplastic and loosely scattered, and while lymphocytes are present in the surrounding tissue they have not definitely infiltrated between the tumour cells. Harvey, Dawson and Innes draw attention to the lymphoid aggregations which form round the tumour cells of seminoma and pinealoma. Digby had never seen a case where lymphocytes occurred in the metastases. In this series none of the post mortem examinations were made on cases with the histological appearance of lymphoepithelioma. Autopsy sections of one case of lymphoepithelioma were studied however and lymphocytes were not present among the epithelial cells in the metastases. Obviously the presence of lymphocytes among carcinoma cells in lymph nodes cannot be accepted as proof of any symbiotic relationship between them. Le Gros Clark has described the proliferation of endodermal cells which takes place in the embryo before the lymphocytes are laid down and how when the lymphocytes appear and also proliferate they come into close association with the endodermal cells, an appearance which is maintained in later life. The epithelial cells of 'lympho-epithelioma' are anaplastic and rapidly growing and



as they infiltrate a stroma rich in lymphocytes it seems only natural that the latter should be incorporated among the tumour cells. Distant spread takes place by embolism and it could be that the embolus broken off from tumour might contain lymphocytes as well as epithelial cells.

Munro Black pointed out that if one is to regard the lymphocytes as a growing part of the tumour one must either accept the entity of lymphoepithelium or classify the tumour as a sarcoma. The solid cords or alveoli of epithelial cells usually served to distinguish these growths as carcinoma. Where the general appearance is sarcomatous careful search usually reveals solid groups of epithelial cells in some part of the tumour. Some of the histological sections taken in cases treated by urethane previous to this study, were lymphoepithelioma and they revealed definite epidermoid characters after urethane therapy. Several cases in which the primary presented the appearance of lymphoepithelioma declared themselves in the cervical metastases as squamous cell carcinoma with no admixture of lymphocytes.

The resemblance between the anaplastic epithelial cells of lymphoepithelioma and the reticulum cells of lymphoid tissue was noted by McKie (1949). Harvey,

Dawson and Innes thought that many lymphoepithelioma were in fact reticulum cell sarcoma and Bonne has described the same tumours as "reticulo endothelioma". While reticulum cell sarcoma must be borne in mind as a possible differential diagnosis of lymphoepithelioma careful study of primary nasopharyngeal tumour and cervical lymph node metastases will give the correct diagnosis in the vast number of cases. Where there is no demonstrable tumour in the nasopharynx, the clinical picture may settle the diagnosis but as Willis points out "complete and careful necropsy study is often the only means of establishing - or refuting - the primary nature of an anaplastic tumour of uncertain nature in a lymph gland".

Clinically lymphoepithelioma did not differ significantly in its behaviour from anaplastic carcinoma without lymphocytes in the appearance of the primary growth frequency of symptoms, of cervical adenopathy, cranial nerve lesions, erosion of cranium or distant metastases. The only difference lay in the fact that lymphoepithelioma arose where there were lymphoid aggregations under the epithelium.

Lymphoepithelioma therefore, falls into place among the anaplastic carcinoma of the nasopharynx and while it presents a variant of the histological picture



there is not enough evidence to regard it as a pathological entity.

In comparing the histology of the two macroscopic types of tumour there was no significant difference between the number of fungating and small lesions which fell into the second and third histological group. Two of the small ulcers were differentiated squamous cell carcinoma, while no fungating lesions fell into Group I. Apart from this, tumours of either gross type could present any given histological picture, and they therefore comprised two varieties of one neoplastic process. The fungating growths made up 70% of all tumours, - they arose slightly more frequently from the roof and posterior wall than from the lateral wall in relation to the small ulcerative lesions. Even in the lateral wall they were twice as common as small lesions. The slightly greater incidence of small ulcers on the lateral wall than elsewhere may be explained by the frequent location of tumours in the fossa of Rosenmüller so that the full extent of a growth may not be visible.

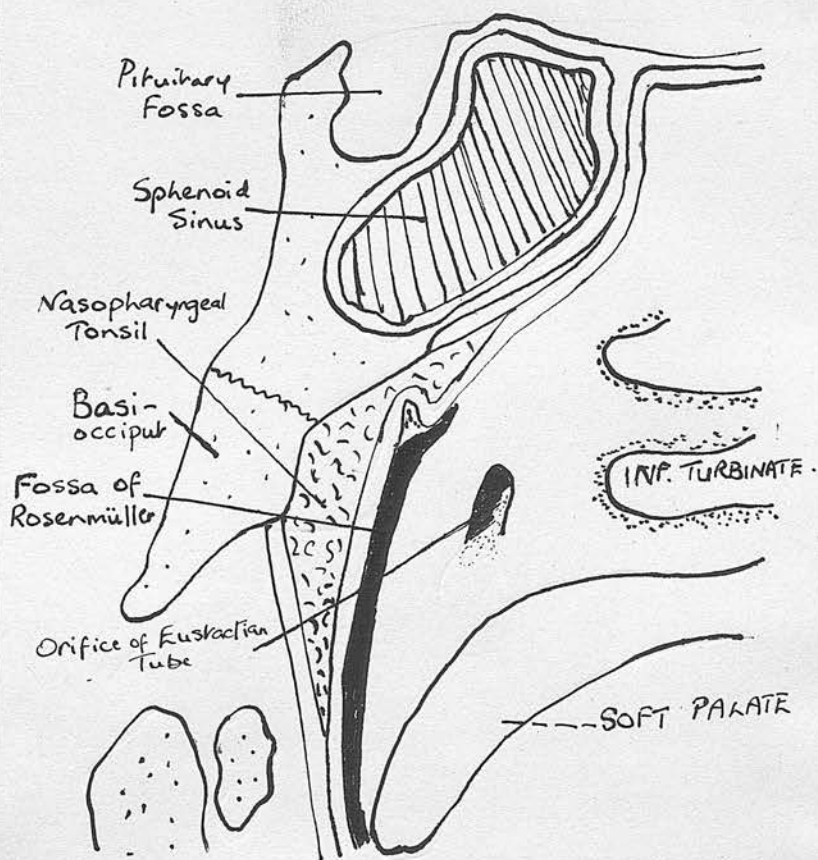
#### Conclusions.

From the study of the histology of the tumours in this series it has become evident that one continuous

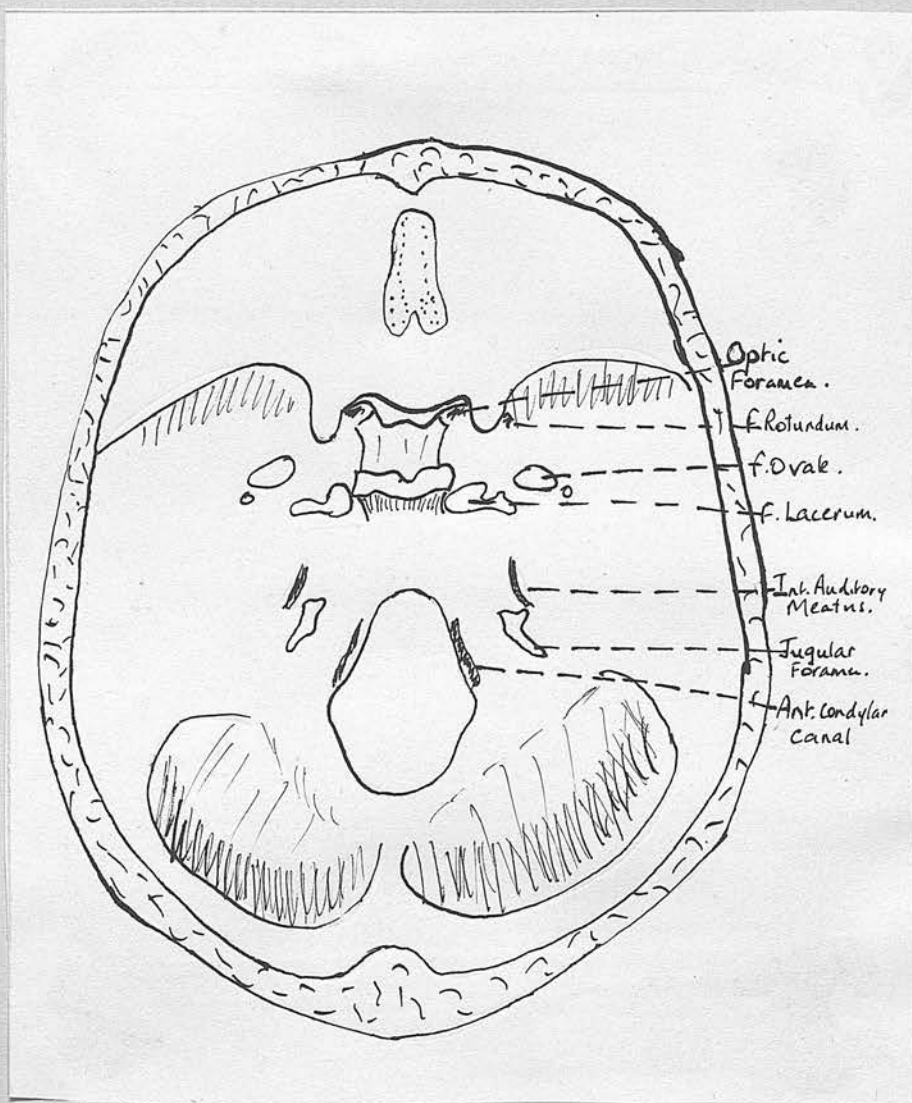


pathological process is at work. It does not appear justifiable to regard transitional cell carcinoma or lymphoepithelioma as separate tumours but rather as variants of one consistent histological picture.

Because of the squamous characters of the more differentiated tumours of this series and of the regularity with which their transition to the less differentiated forms can be traced they are all regarded as squamous cell carcinoma of varying degrees of differentiation. The absence of cornification in any of these tumours is explained by the normal squamous epithelium lining the nasopharynx which is of a stratified type which does not cornify.

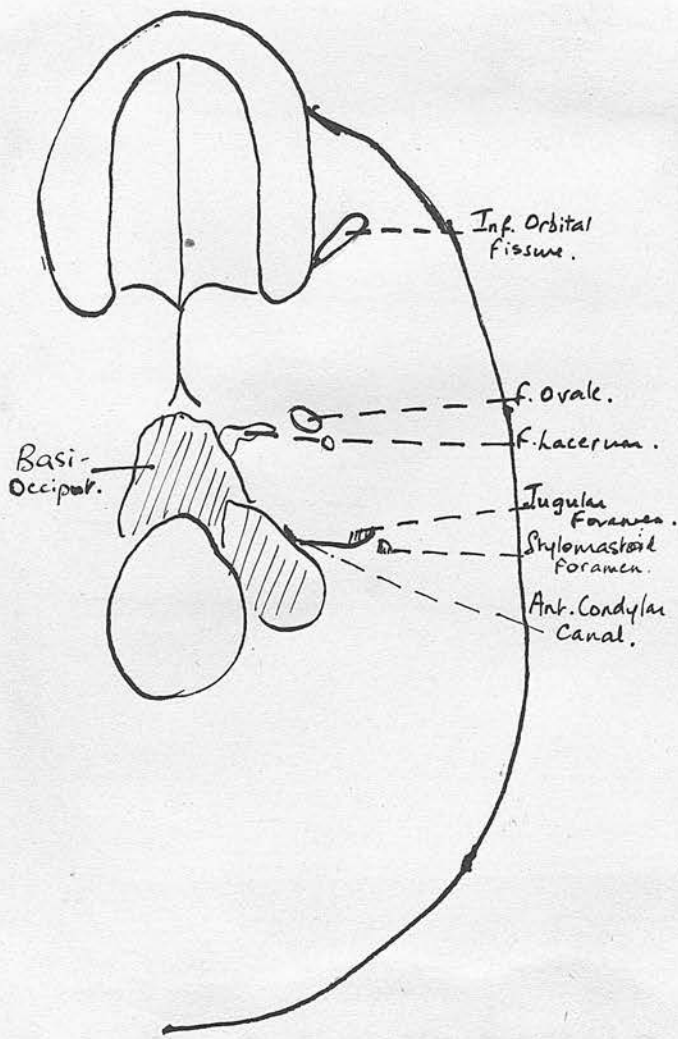


# I. The Nasopharynx.

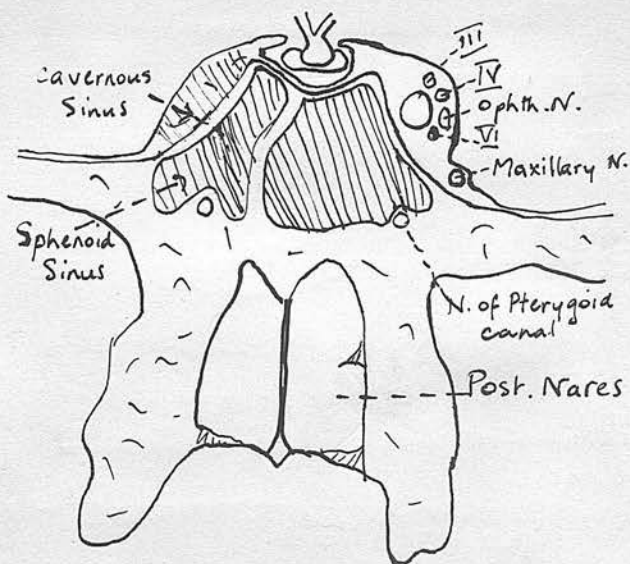


2. Base of Skull from above.

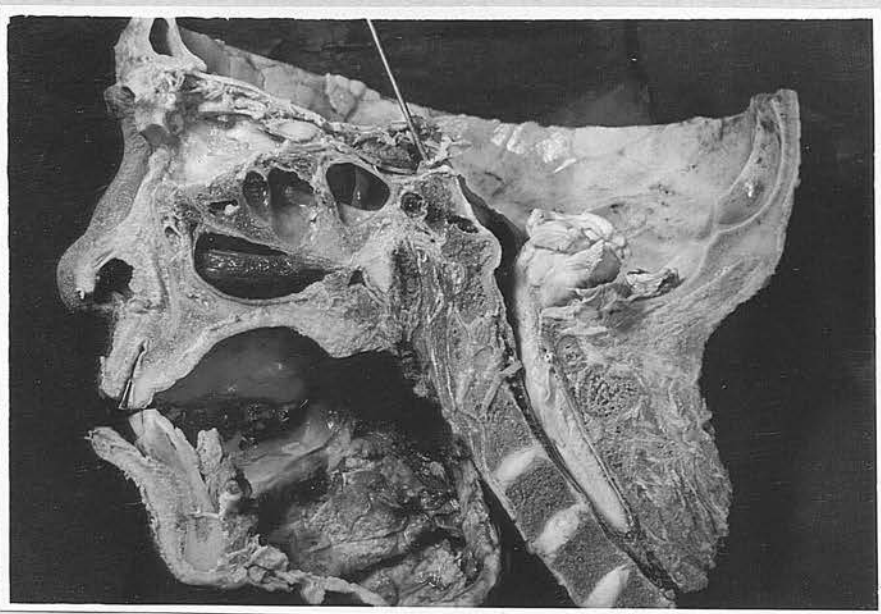




3. Base of Skull from below.



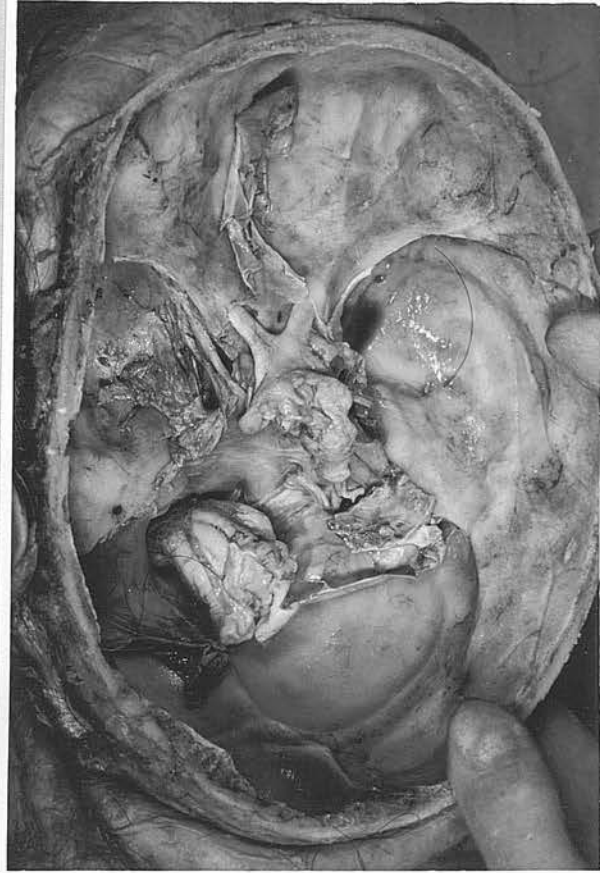
4. Sphenoid and Cavernous Sinuses.



5. Dissection of Skull. Probe in Foramen  
Lacerum.



6. Dissection of Nasopharynx.  
Soft palate is being held forward  
by match-stick. Probe entering  
lower part of Fossa of Rosenmüller.

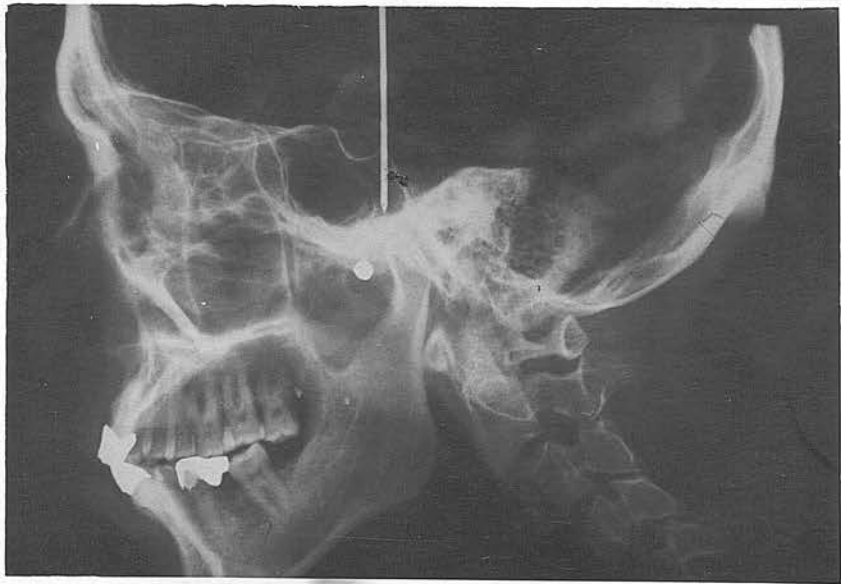


7. Dissection of base of Skull seen from above.



8. Dissection of Nerves of Cavernous Sinus.

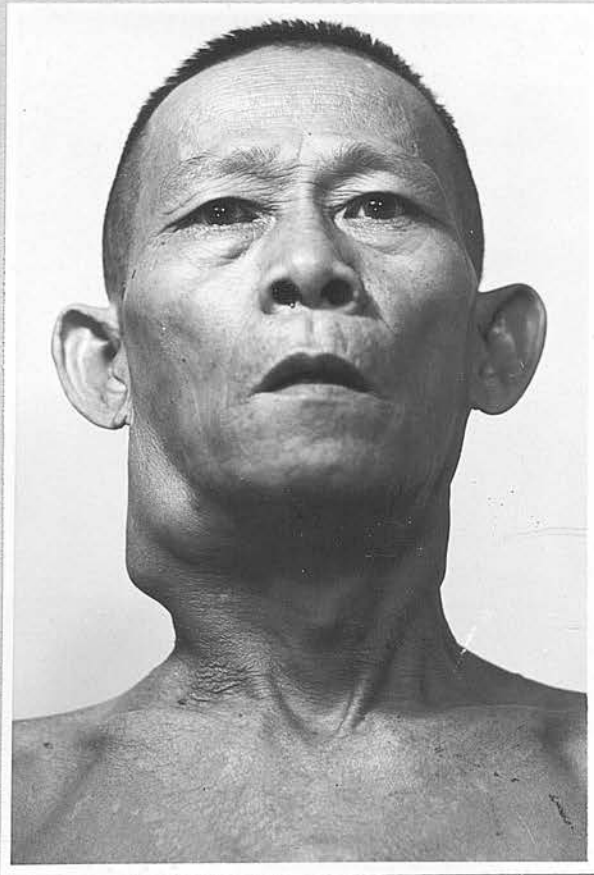




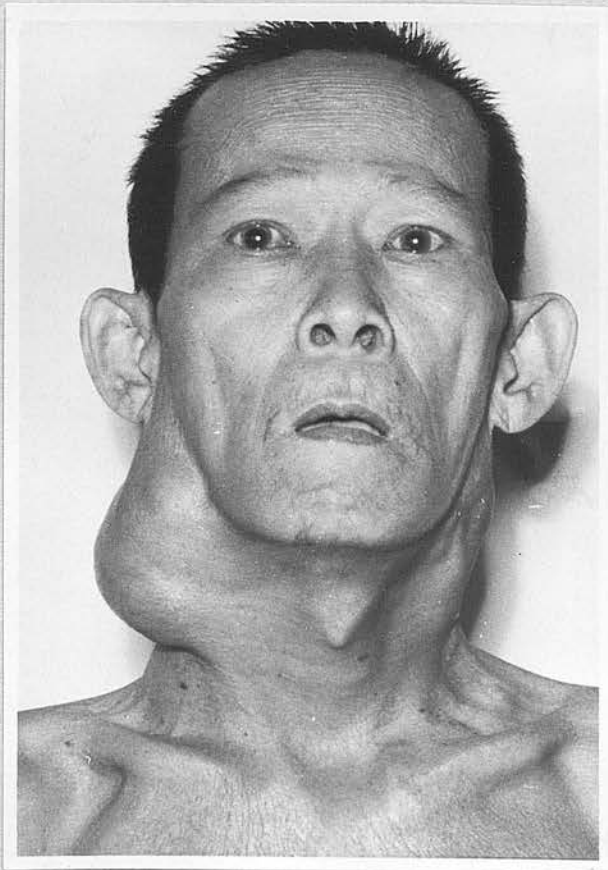
9. Lateral view of dissected Skull  
with probe in Foramen Lacerum and  
metal pellet in Fossa of  
Rosenmuller.



10. Basal view of same.



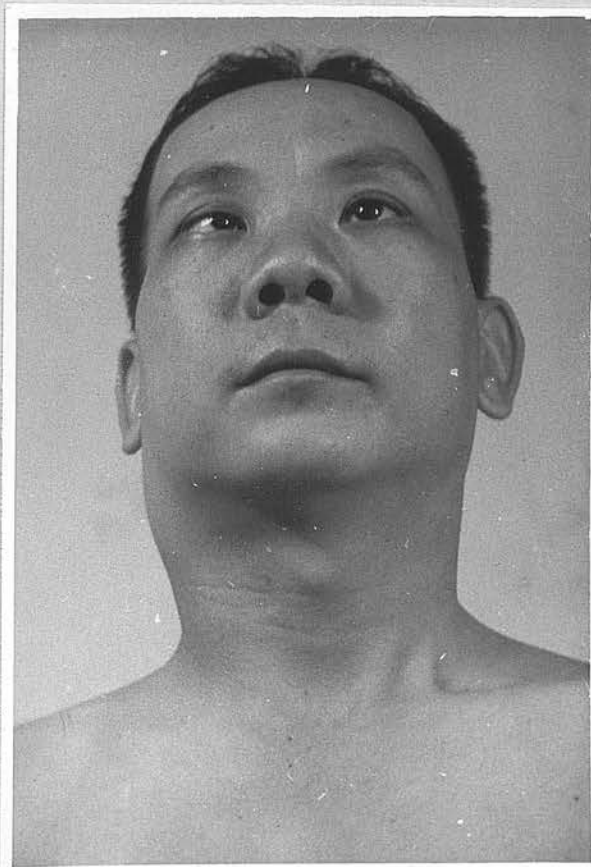
II. Case 2. Bilateral asymmetric Cervical Adenopathy.



12. Case 2. Untreated 9 months later. Adenopathy increased. Patient had become emaciated.



I3. Case 2. Metastasis in Second Cervical Vertebra.



I4. Case 4. Before Urethane.  
Internal Strabismus on right.





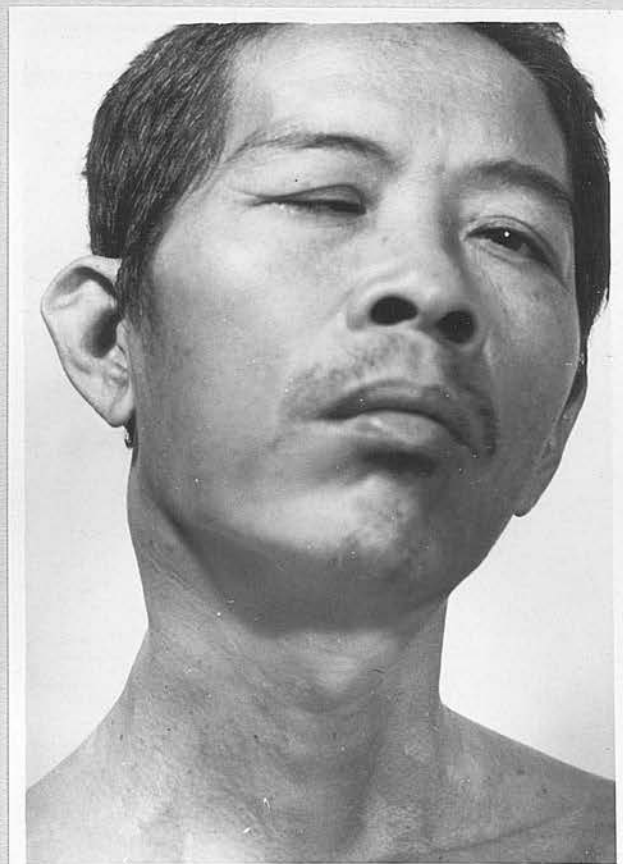
15. Case 4. After Urethane.  
Adenopathy gone.



16. Case 4. Extensive erosion of Rt.  
Middle Cranial Fossa.



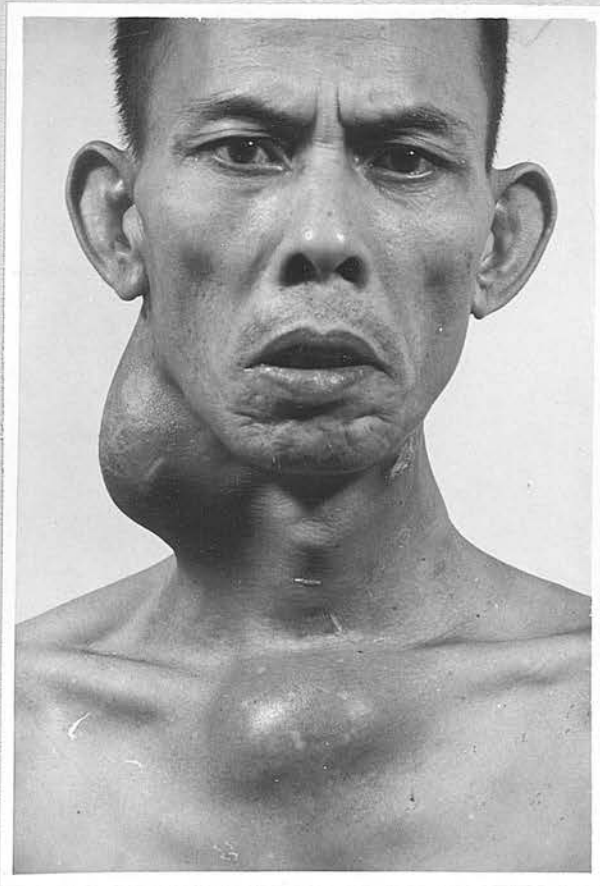
I7. Case 4. Invasion of Sphenoid Sinus.  
Destruction of Sella  
Turcica and posterior wall  
of orbit.



I8. Case 6. Ptosis on right. Concurrent  
lesions of Rt. VI and Ist.  
and 2nd. divisions of V.  
Also Rt. XII. Lesion.

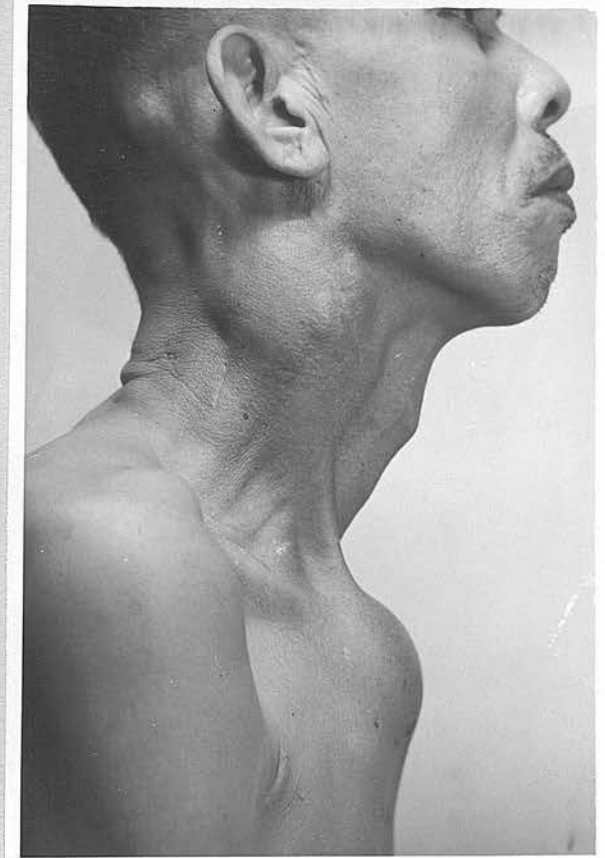


19. Case 6. Enlargement of Pituitary fossa  
with marked erosion of  
posterior Clinoid processes.

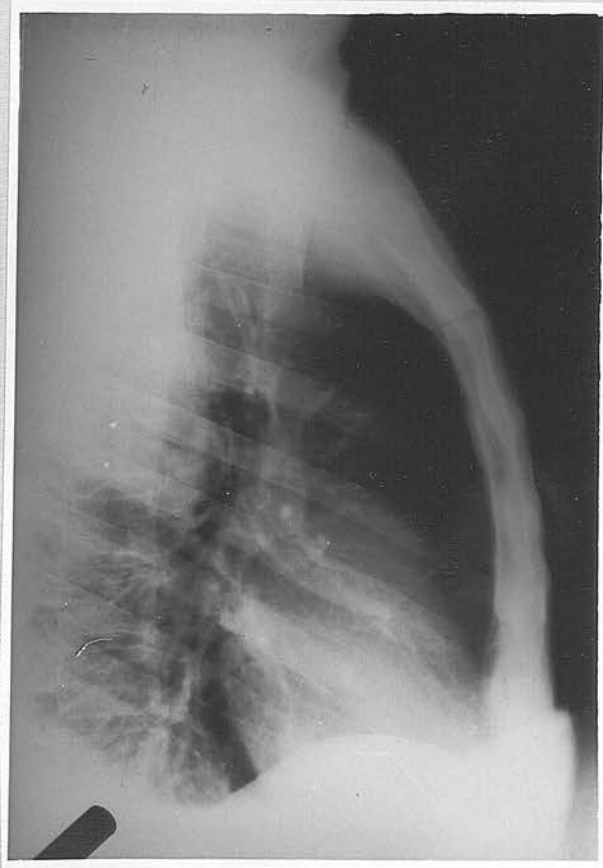


20. Case 8. Sternal Metastasis.

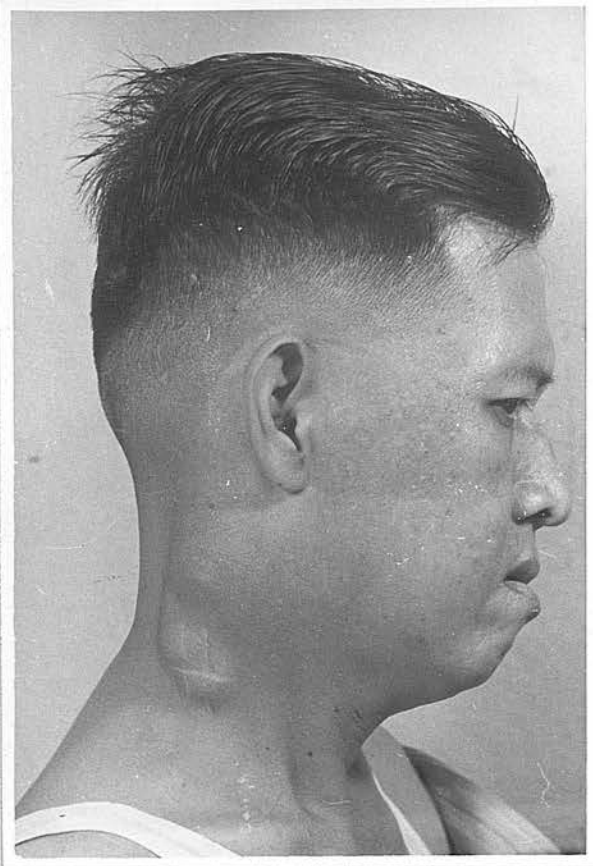




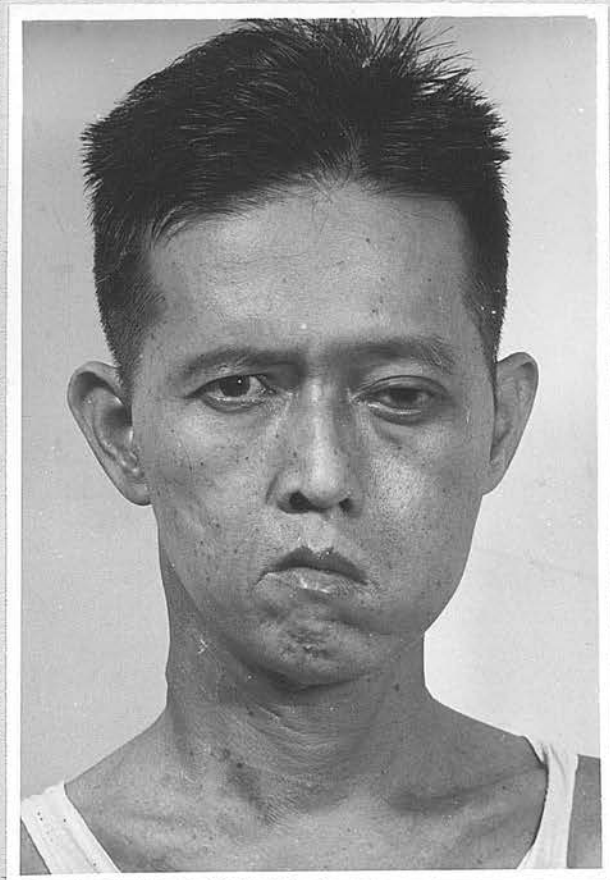
21. Case.8. Lateral view of Sternum.



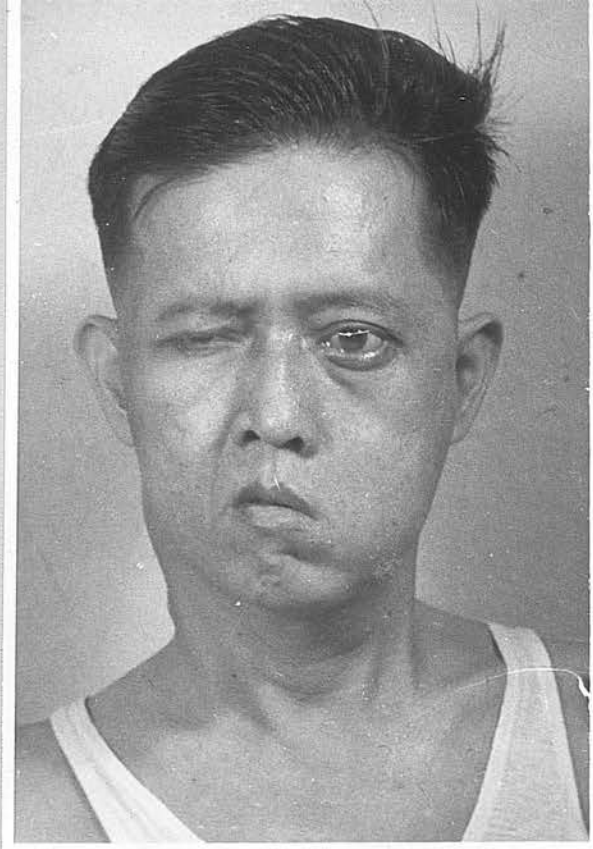
22. Case 8. Lateral Radiograph of chest  
showing Sternal Metastasis.



23. Case 20. Before Urethane.



24. Case 20. After Urethane. Left ptosis  
and proptosis. Lt. facial  
paralysis.



25. Case. 20. 2 months later. Glands recurring. Lt. proptosis worse. Rt. ptosis.



26. Case 20. 6 months later. Radiotherapy behind orbit for failing vision had improved rt. ptosis. Glands larger. Keratitis lt. eye.

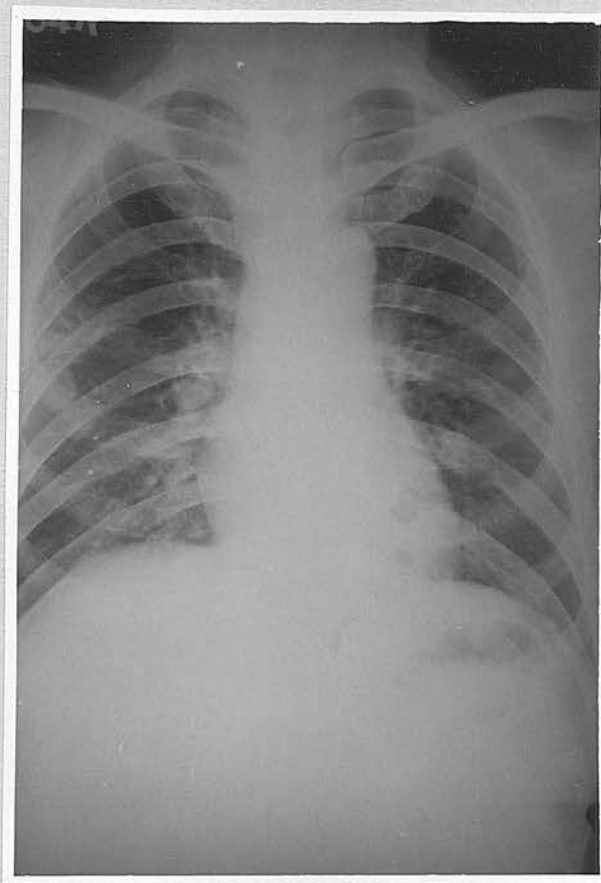




27. Case 20. 13 months later. Massive bilateral erosion middle cranial fossa. Note metastasis with surrounding calcification antero-lateral part of rt. middle fossa.



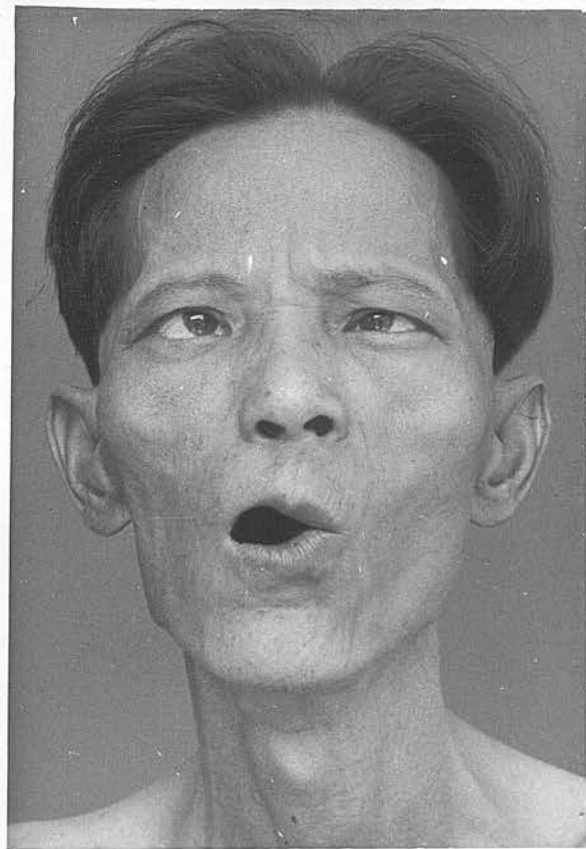
28. Case 20. Same time as 25. Metastases in vault of Skull.



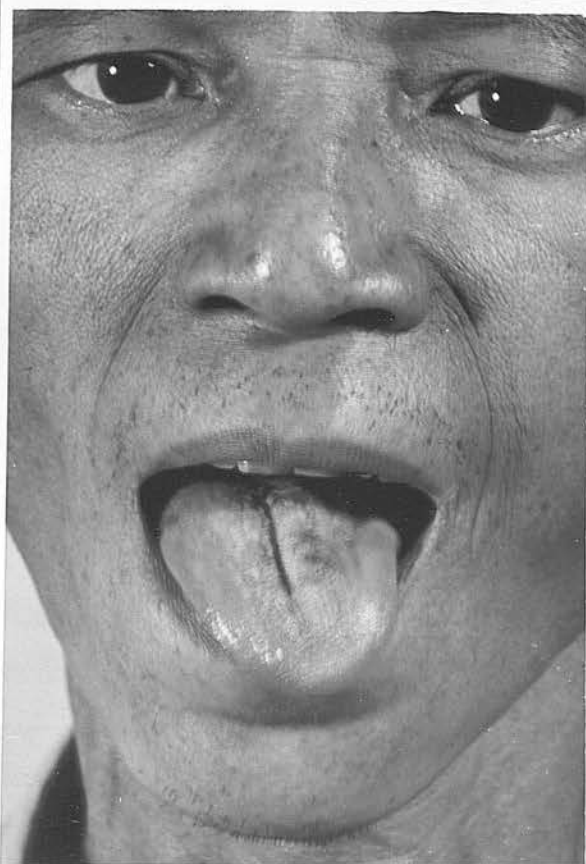
29. Case 20. 2 months later. Pulmonary metastases.



30. Case 23. Early case with Nasopharyngeal tumour and no lymph node metastases.



31. Case 23. 18 months later. Lesions of rt. VI and motor division of V.



32. Case 23. Same time as 31. Lesion Rt. XIV.

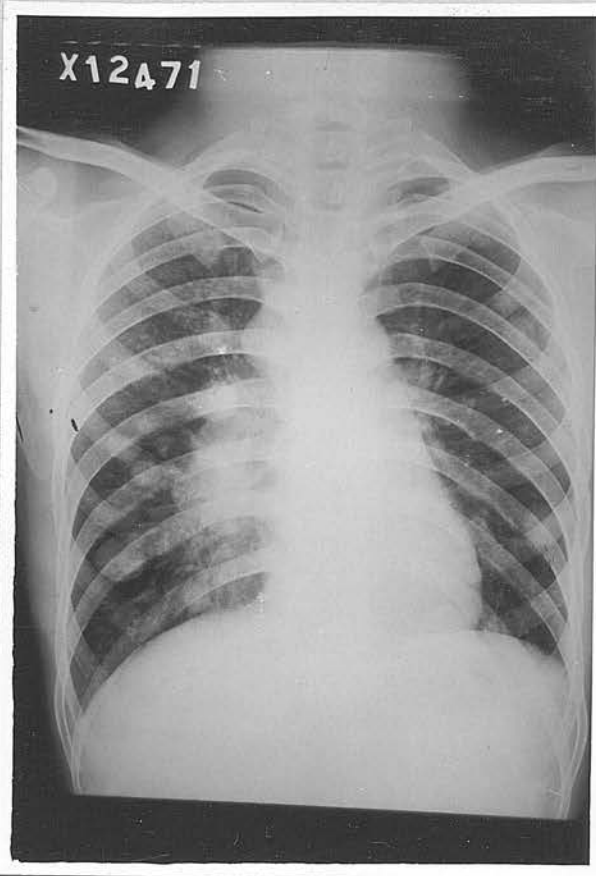




33. Case 27. Thickening of posterior nasopharyngeal wall.



34. Case 27. Metastases in rt. Sacro-iliac joint and acetabulum.



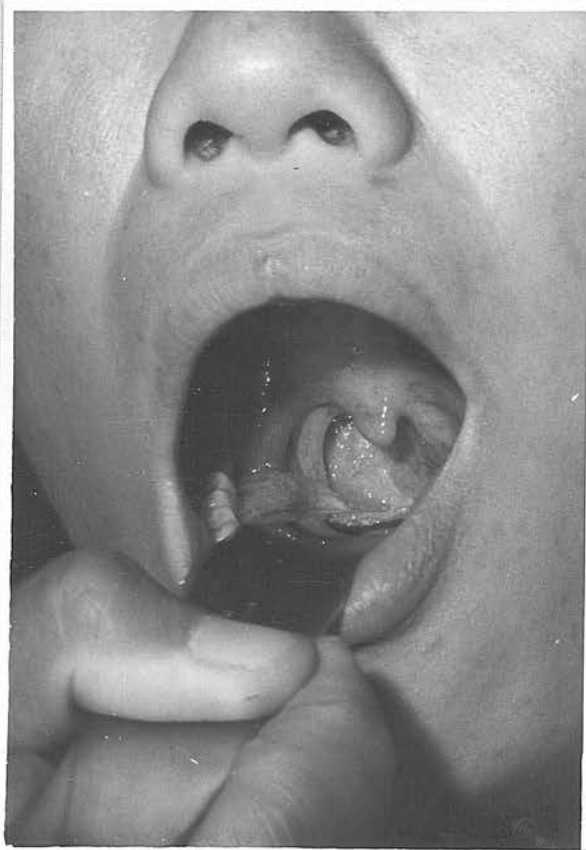
35. Case 29. Pulmonary Metastases



36. Case 35. Bilateral ptosis. Unable to close jaw.

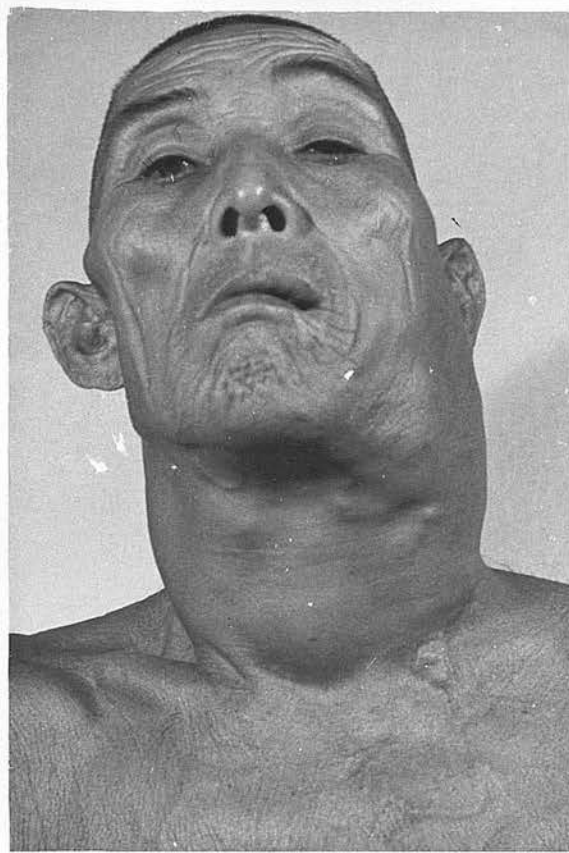


37. Case 39. Left cervical adenopathy.  
Combined carcinoma and tuberculosis.

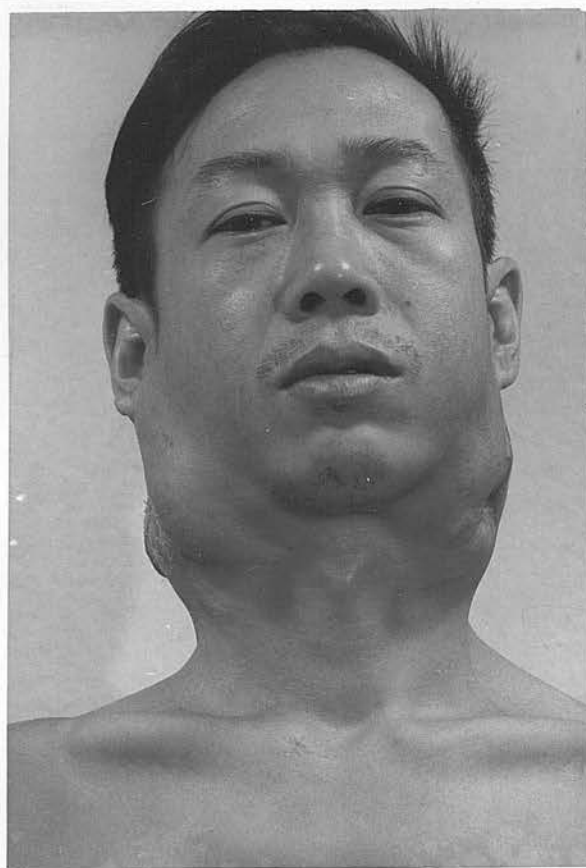


38. Case 39. Fungating tumour in the  
nasopharynx.





39. Case 40. Gross cervical adenopathy on  
lt. extending over midline and  
involving Rt. anterior triangle.  
The Thryoid Gland was infiltrated  
by the tumour.



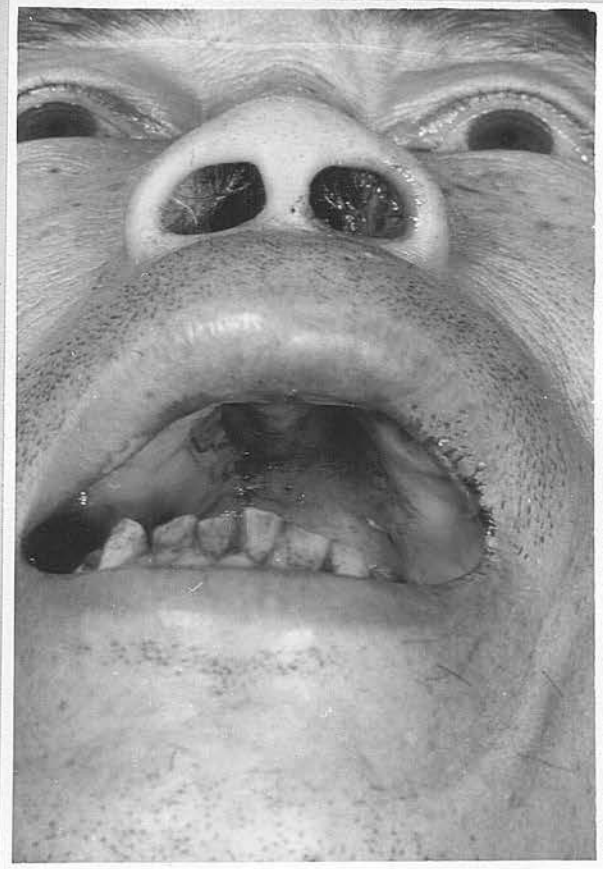
40. Case 45. Gross bilateral Lymphadenopathy.



41. Case 45. After radiotherapy only minimal response to treatment. Retreatment evoked no response at all. Rt. VI lesion now evident.



42. Case 45. Herpes Zoster in distribution of C5-C7 following radiotherapy.

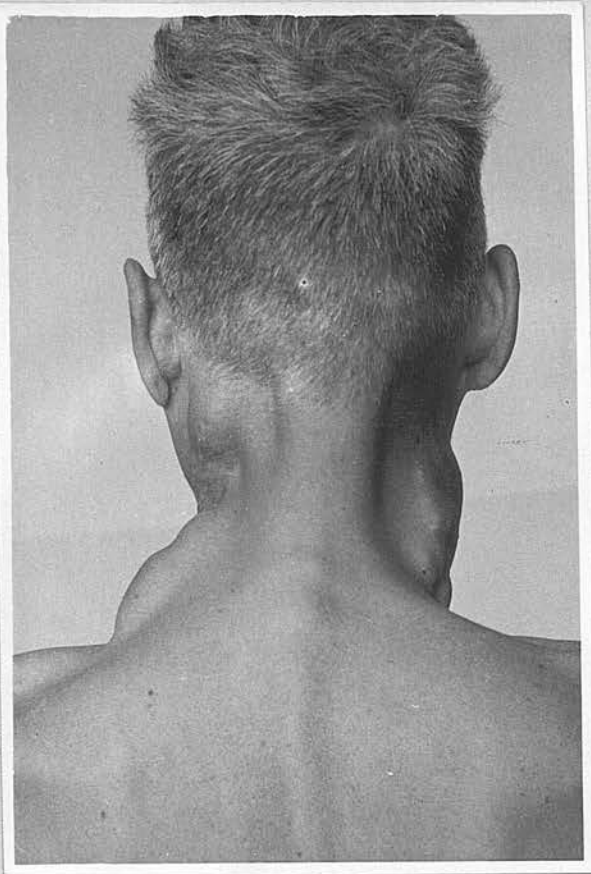


43. Case 55. Palate depressed on rt. by tumour.

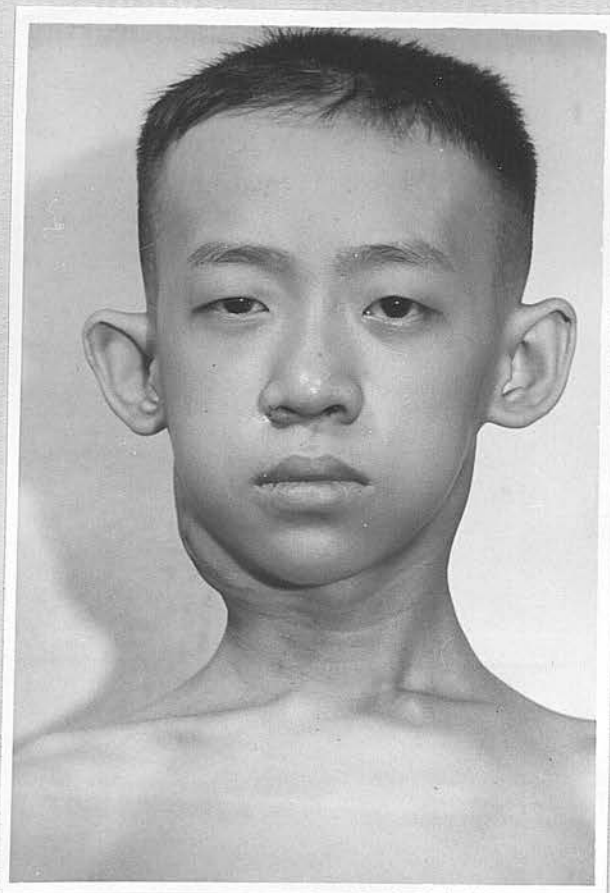


44. Case 55. Osteoblastic Metastasis of Humerus  
demonstrated 10 months after onset of the disease

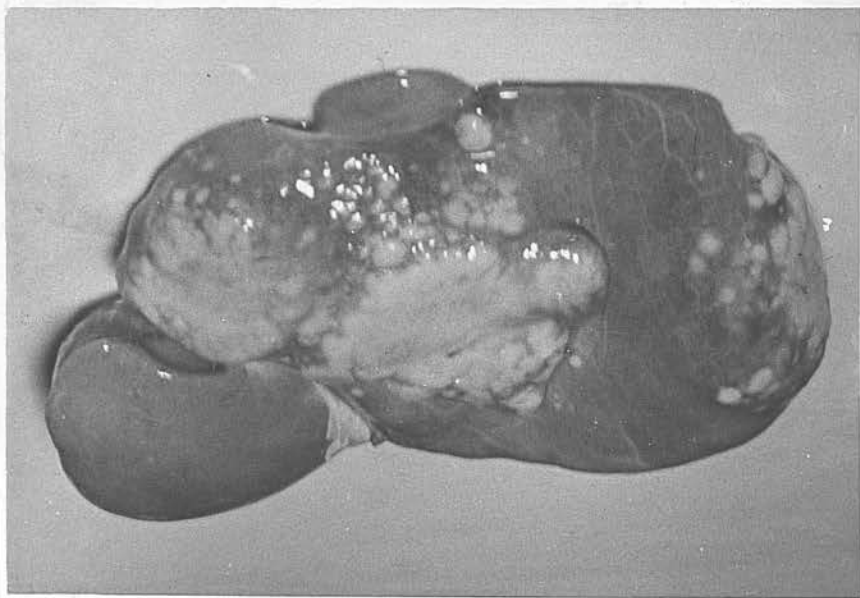




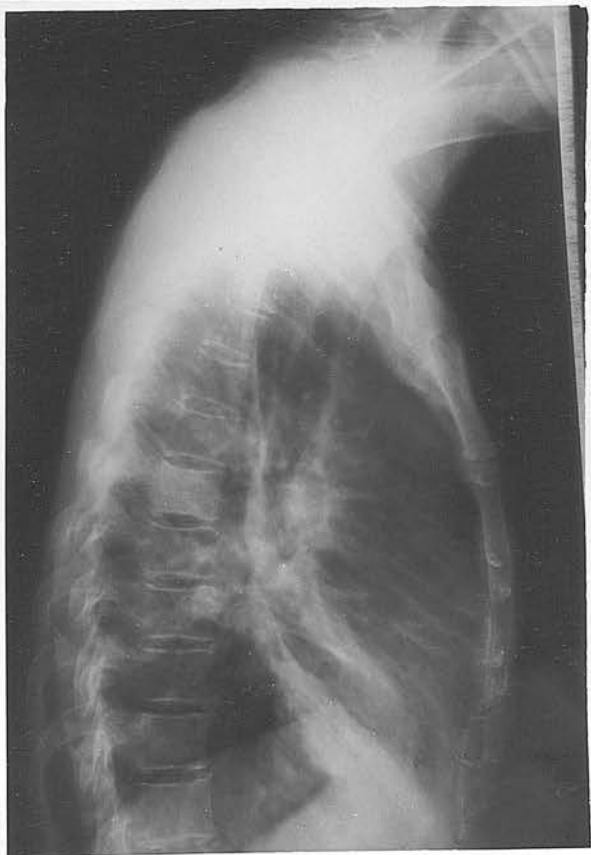
45. Case 58. Lymph node metastases in posterior triangle causing wasting of lt. trapezius.



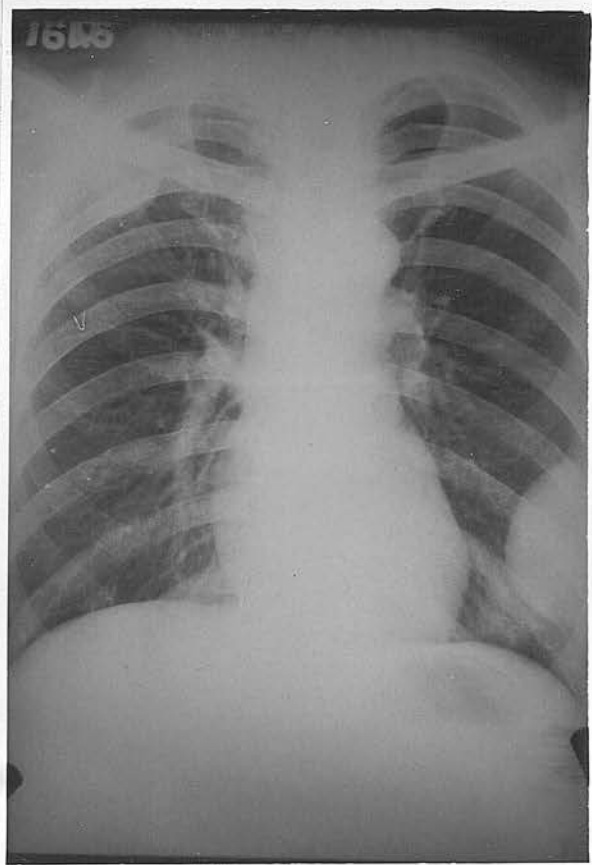
46. Case 61. The youngest patient, aboy of 12 years.



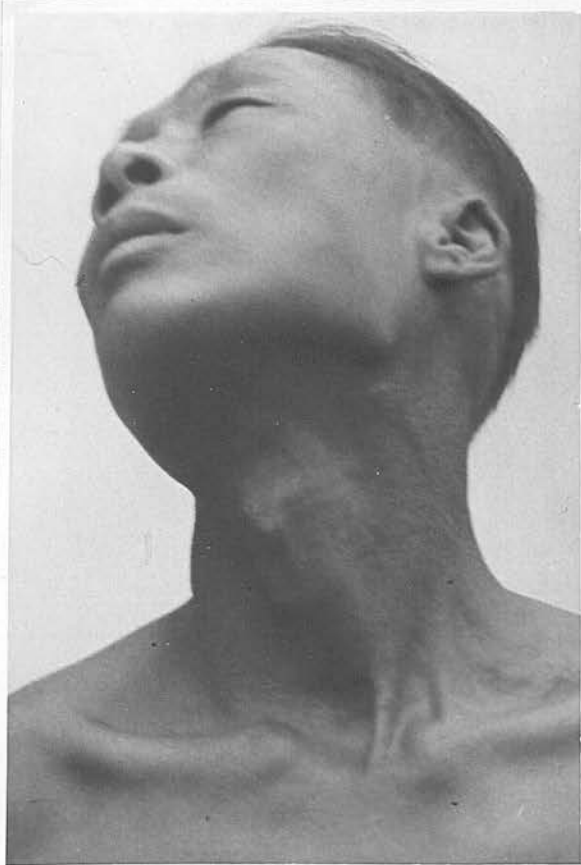
47. Case 62. Liver metastases found at post-mortem.



48. Case 63. Osteosclerotic deposit in sixth dorsal vertebra.

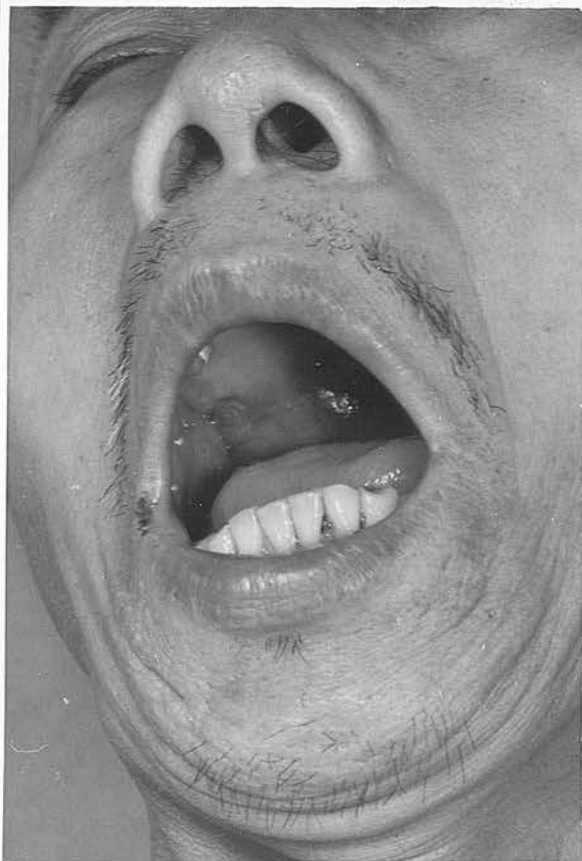


49. Case 79. Large secondary deposit in lt. 2nd. rib.

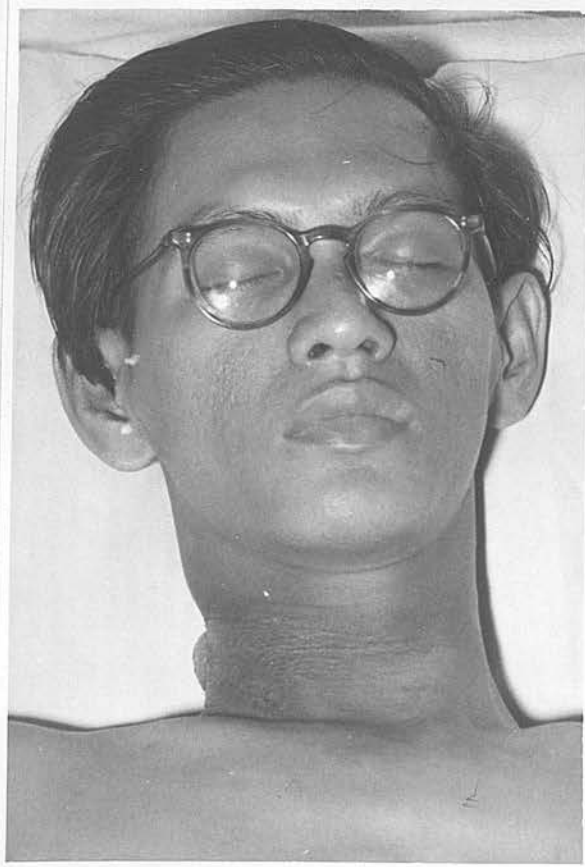


50. Case 83. Wasting of lt. sternomastoid.





51. Case 84. Palate depressed and paralysed by tumour on right.



52. Case 90. Before Urethane. Radioresistant case.



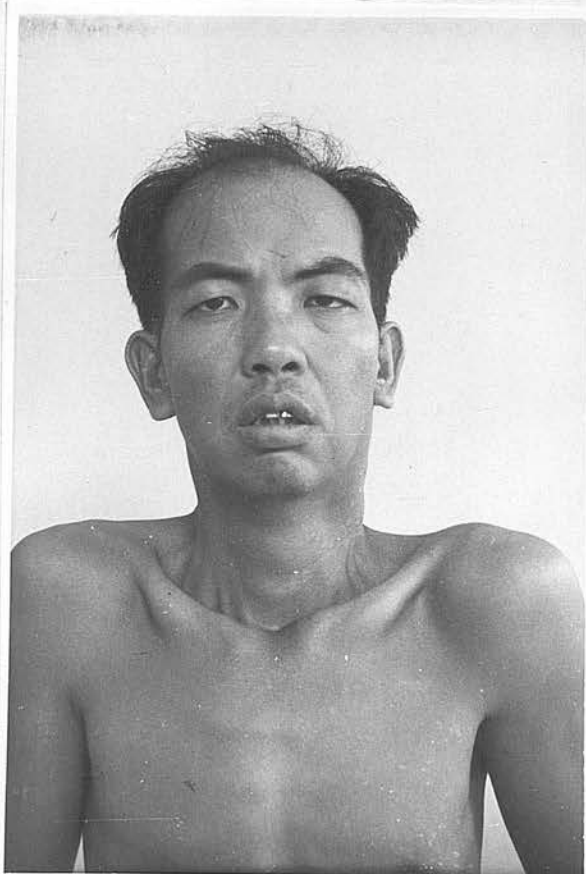
53. Case 90. After urethane. Slight diminution in size of gland.



54. Case IO9. Metastasis involving shoulder joint and eroding clavicle, acromium and humerus with destruction of acromio-clavicular joint.

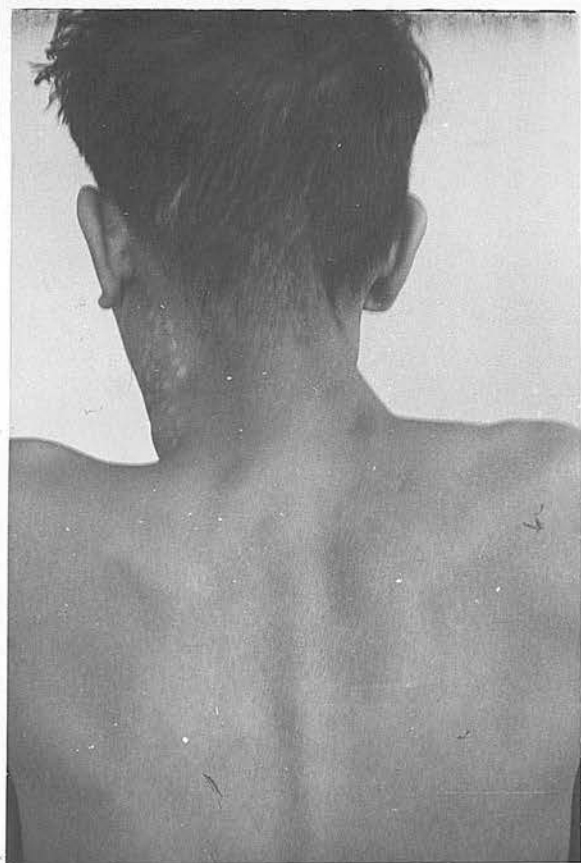


55. Case II0. Result of local application of  
"Chinese Medicine" to Glandular metastases.

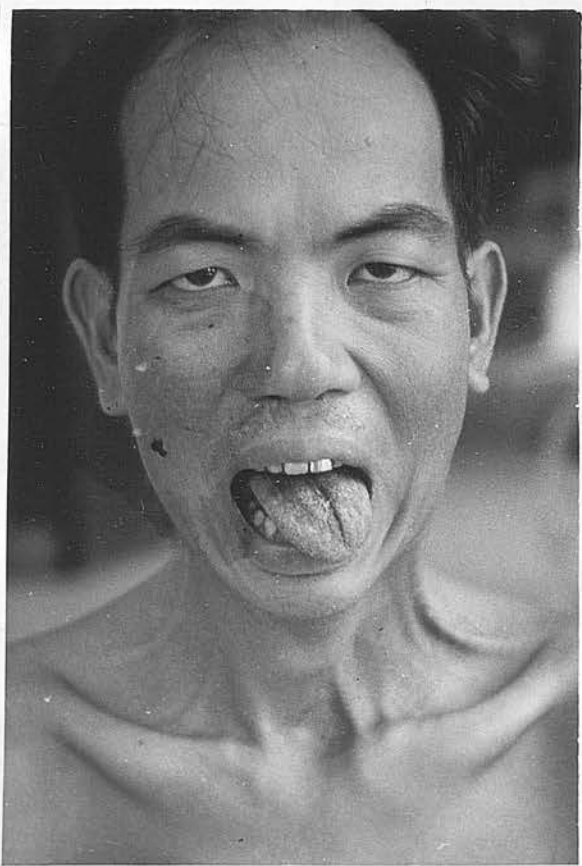


56. Case III. Wasting of left trapezius due to  
lesion of XIth. Nerve. ( Seen from the front ).





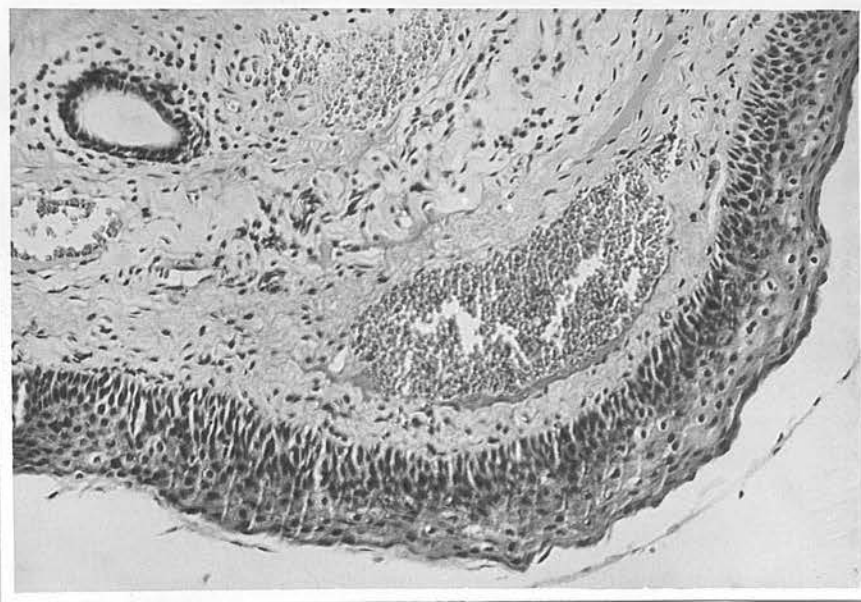
57. Case II2. The same from the rear.



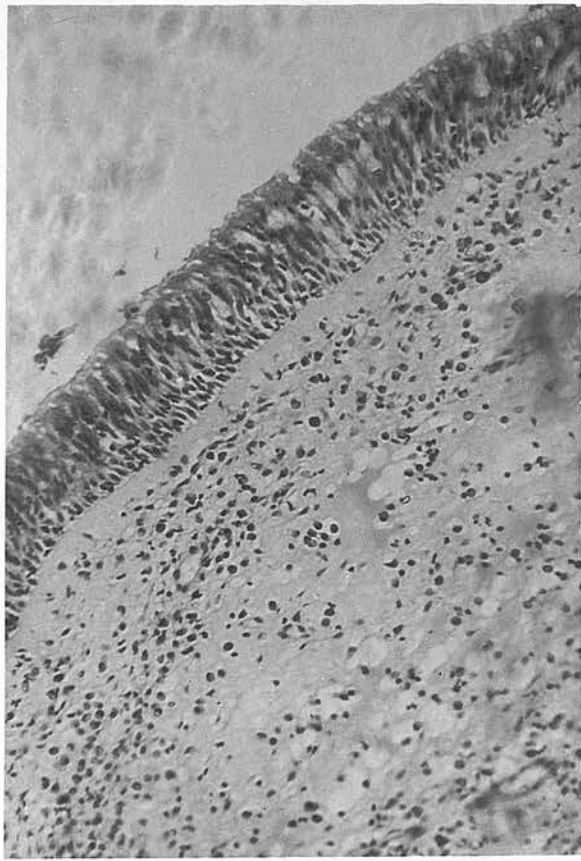
58. Case II2. Hypoglossal paralysis. Paraly



59. Squamous epithelium lining normal nasopharynx.  
x 50.



60. Squamous epithelium X 180.

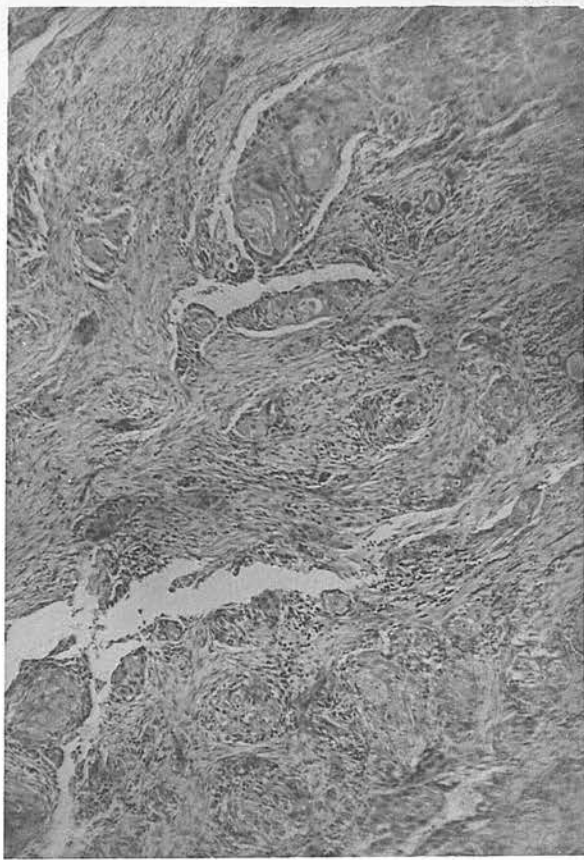


61. Ciliated columnar epithelium of normal Nasopharynx. X 180.



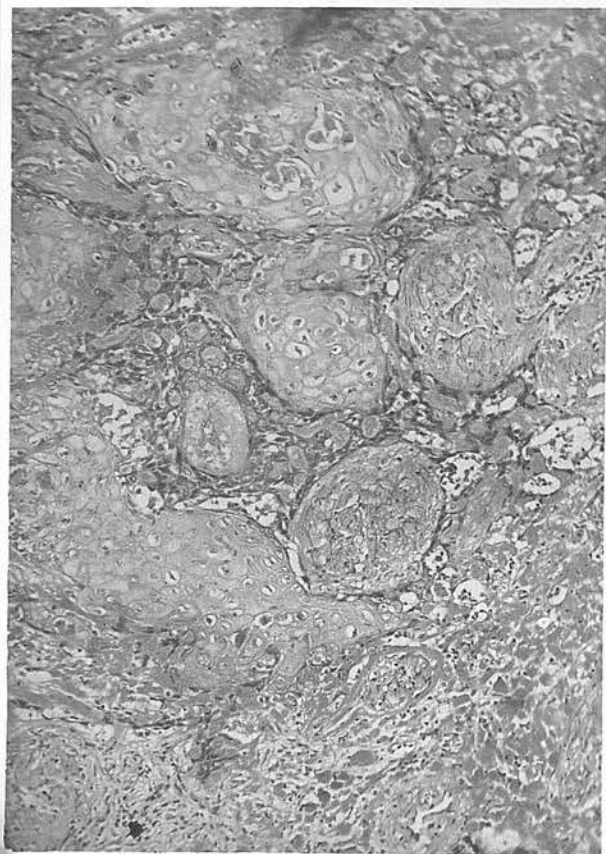
62. Squamous epithelium becoming thinned out over lymphoid tissue. X 180.



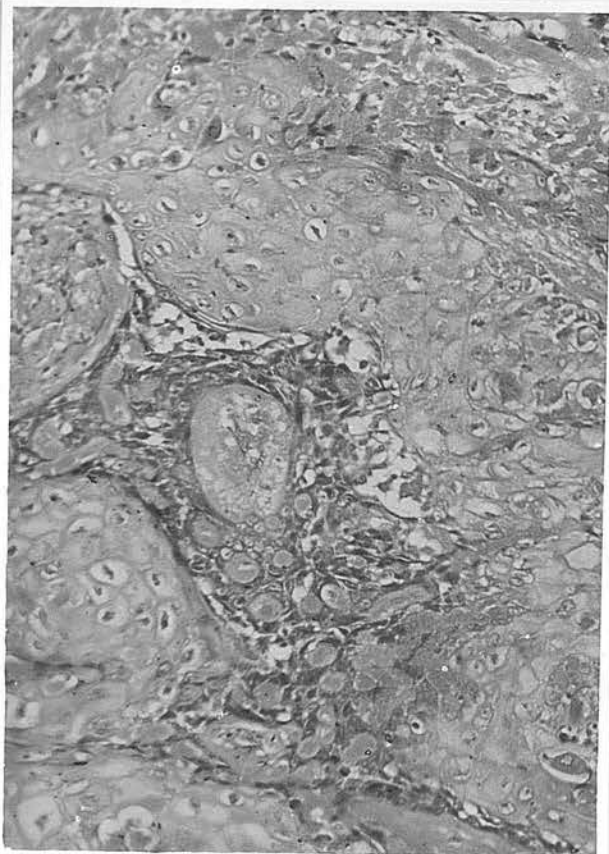


63.Gp. I. Differentiated squamous epithelioma.

X 50. ( case 95).



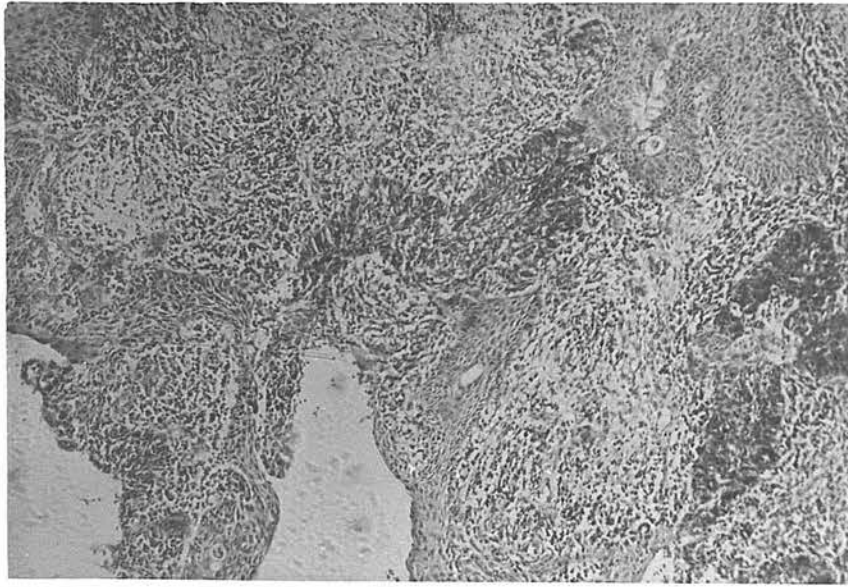
64. Differentiated squamous epithelioma X 100.  
( case 17).



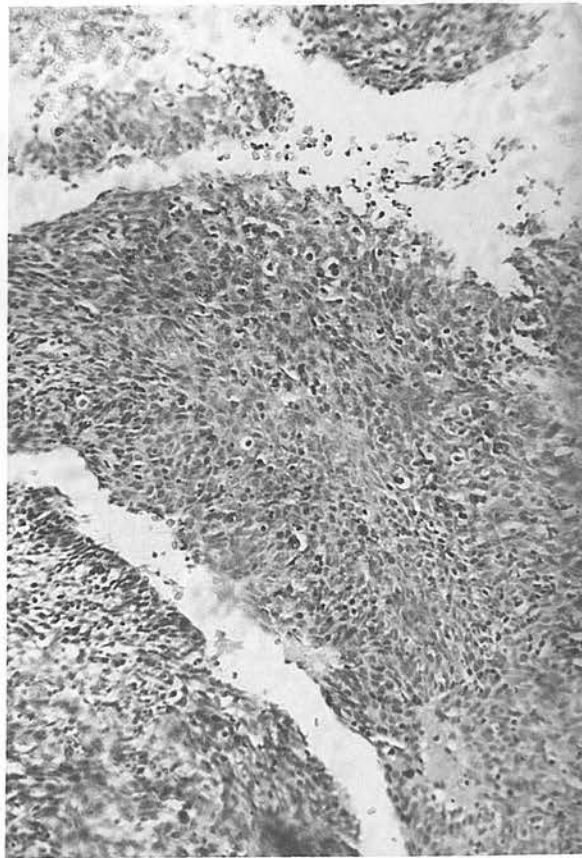
65. Same X 180.



66. Gp.II. Multi-focal origin from squamous epithelium. X 50. (case 59).

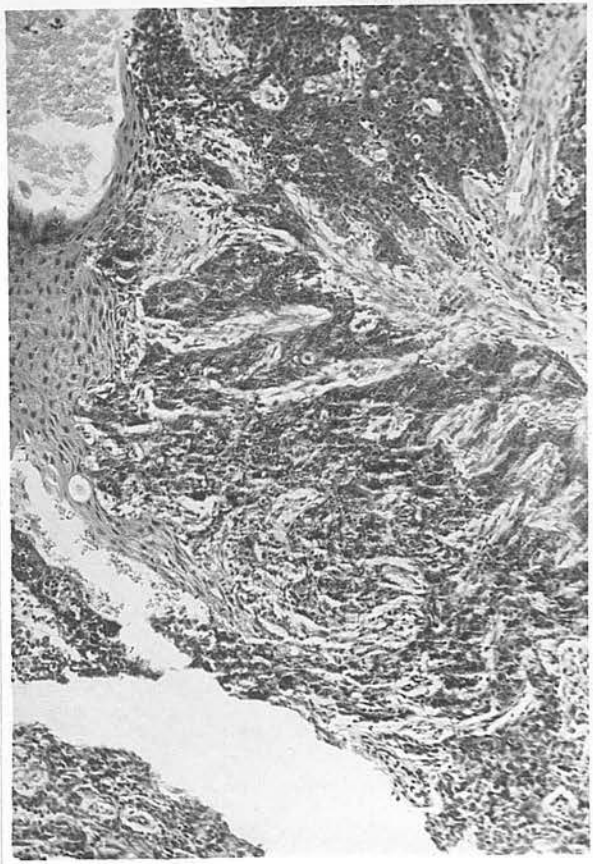


67. Another part of the same tumour. X 50.

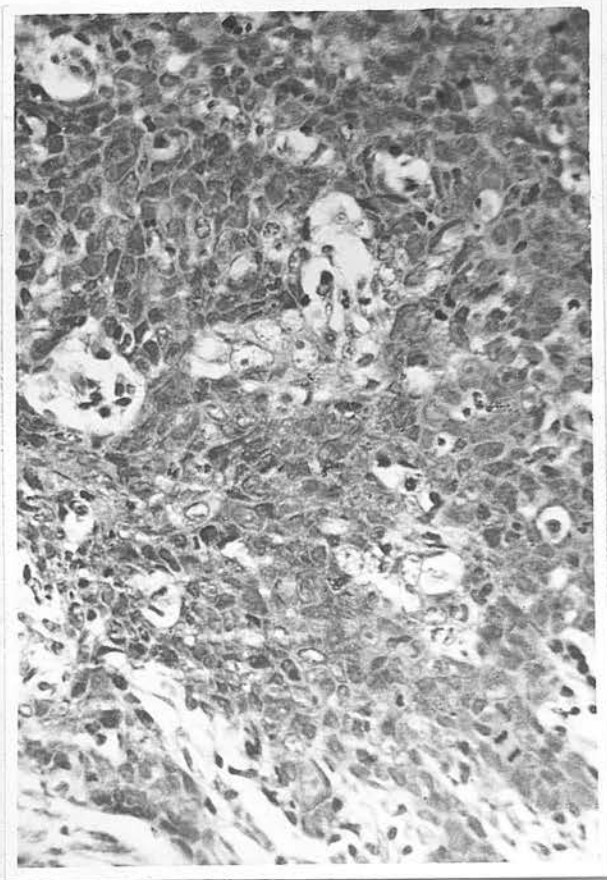


68. Tumour cells of the same by 180.

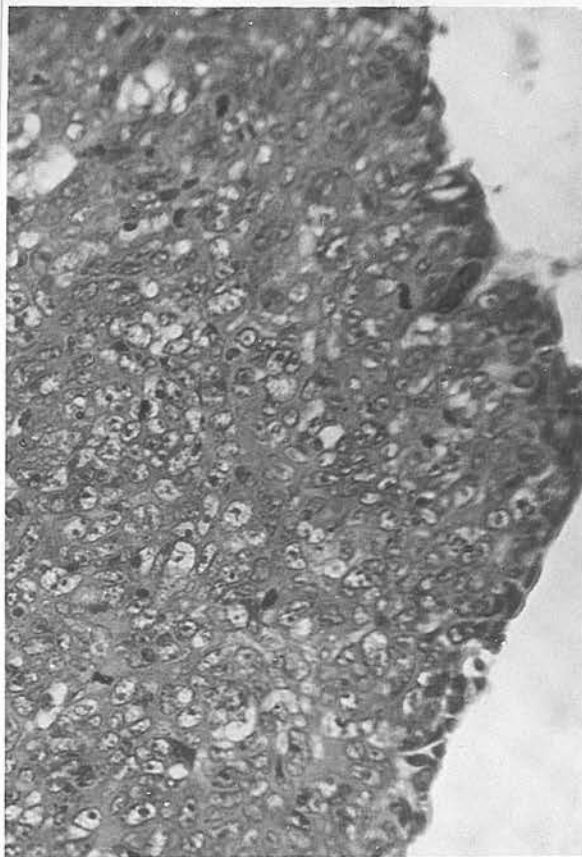




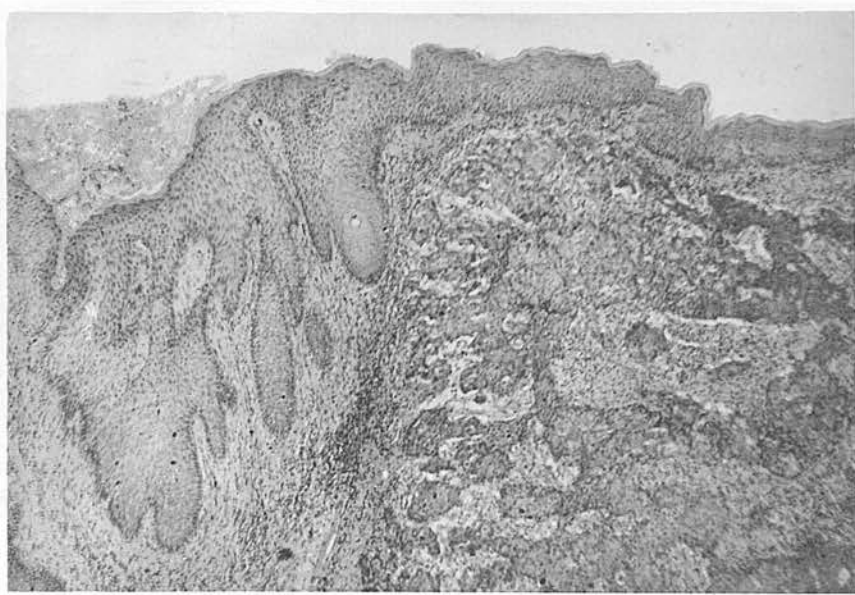
69. Carcinoma arising from the deep layers of squamous epithelium. (case 97).



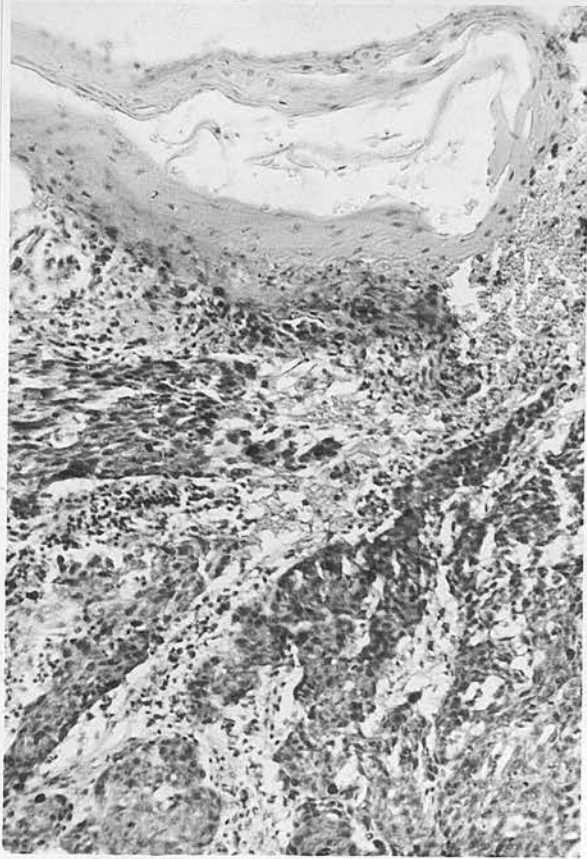
70. Tumour cells of the same. Moderately staining nuclei. X 300.



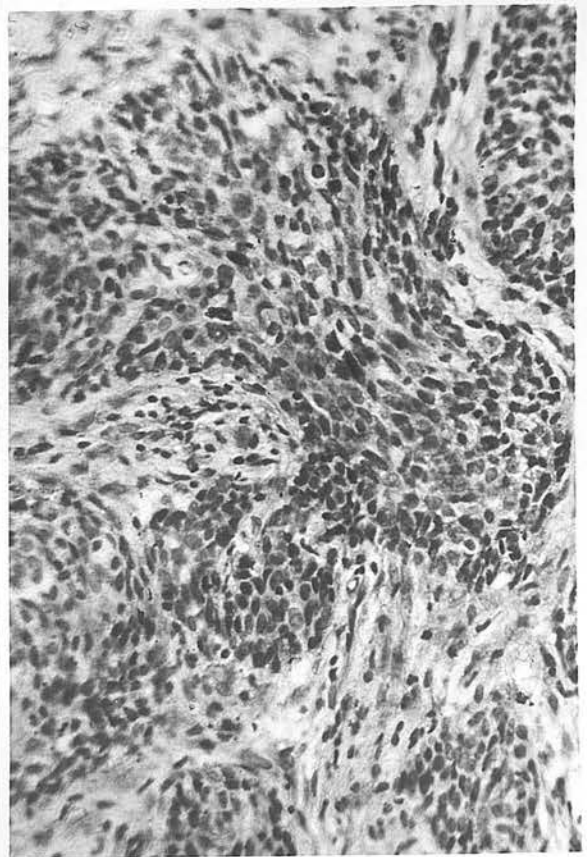
71. Another part of the same. Cells more anaplastic with large vesicular nuclei. X300.



72. Squamous epithelium becoming invasive in the region of the tumour. X 50.

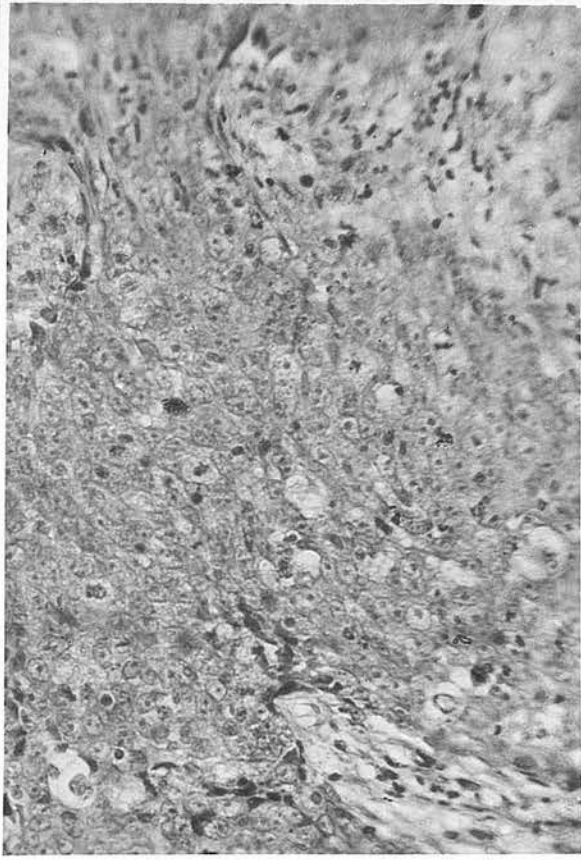


73. Same case. Carcinoma from the deep layers of the epithelium. X 50.

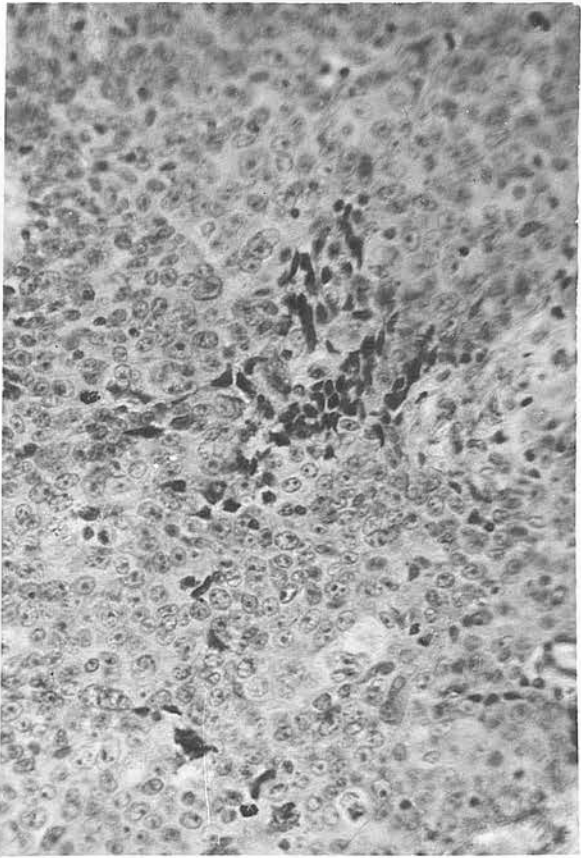


74. Same case. Cells with dark staining spindle-shaped nuclei. X200.

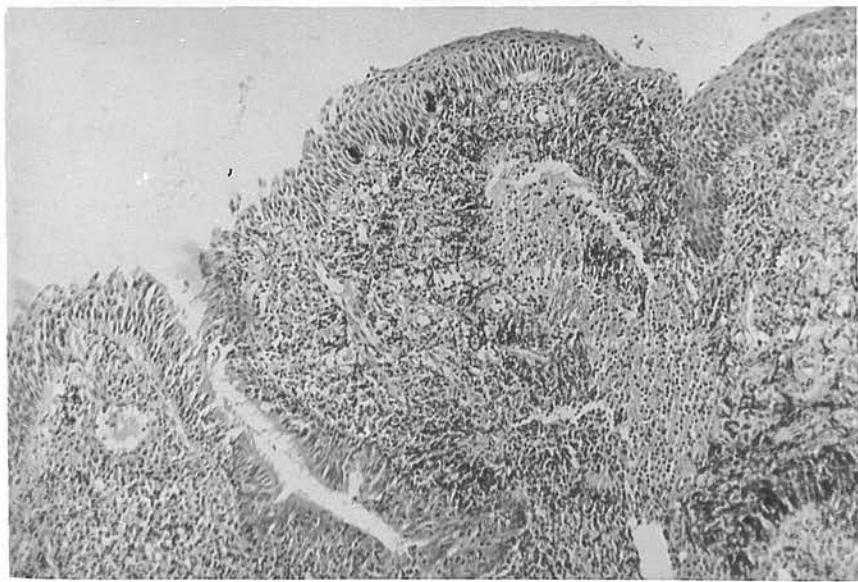




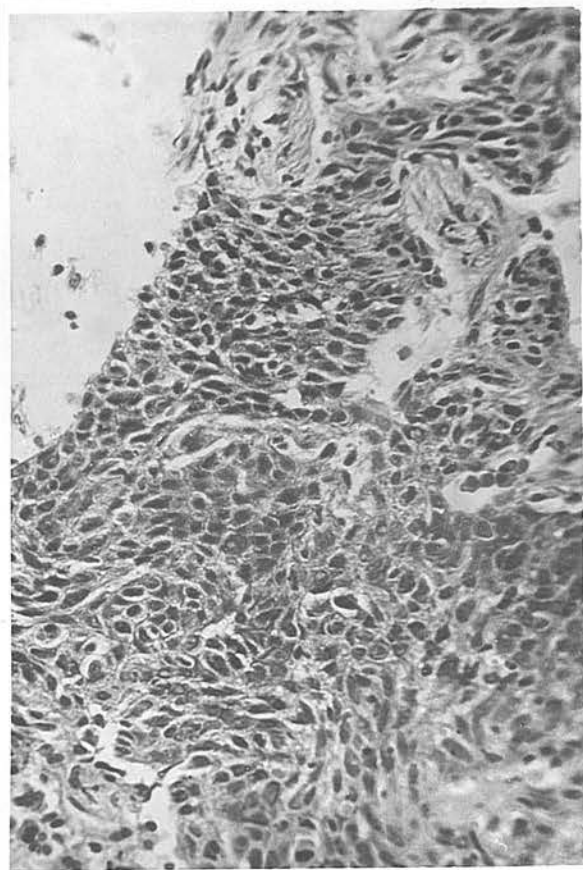
75. Same case. More anaplastic area. Cells with vesicular nuclei. Frequent mitotic figures. X 300



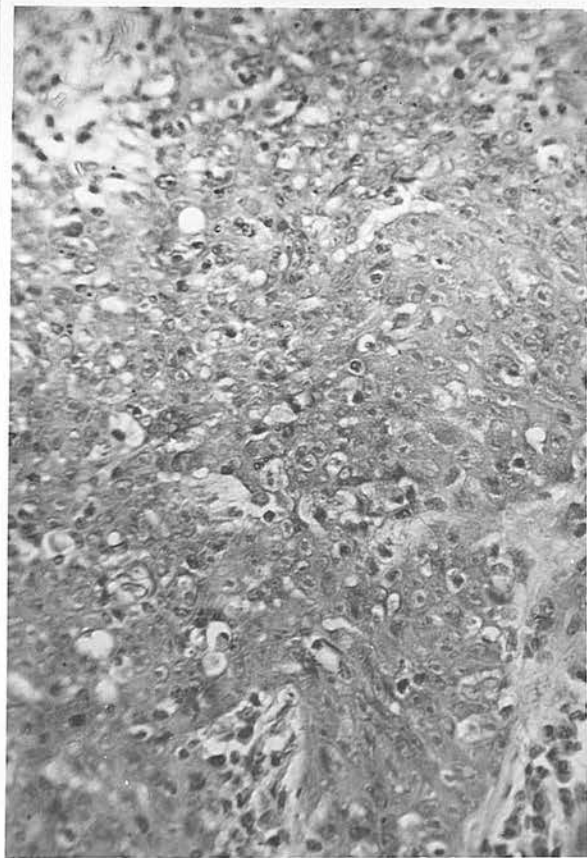
76. Same case. More anaplastic still resembling sarcoma. X300.



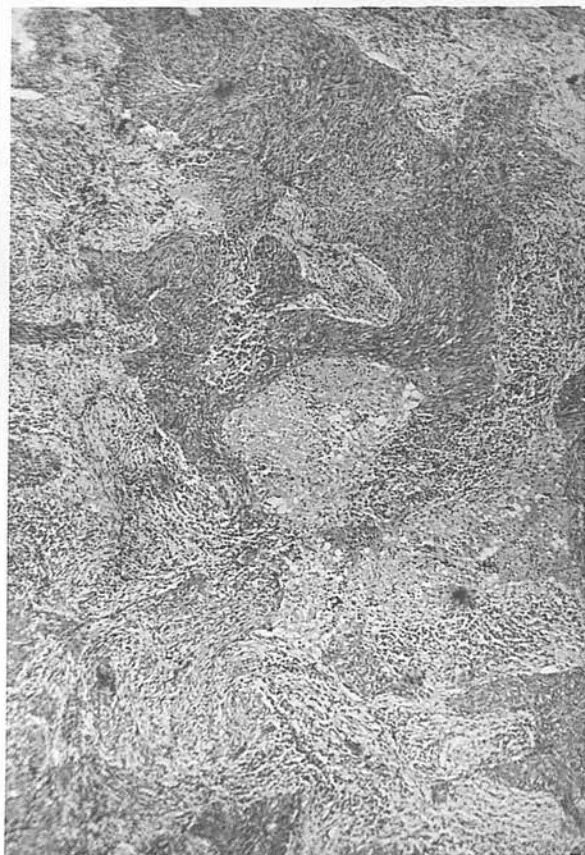
77. Origin from squamous epithelioma. X 50. (case 67)



78. Same case. Tumour cells with dark staining nuclei. X 300.

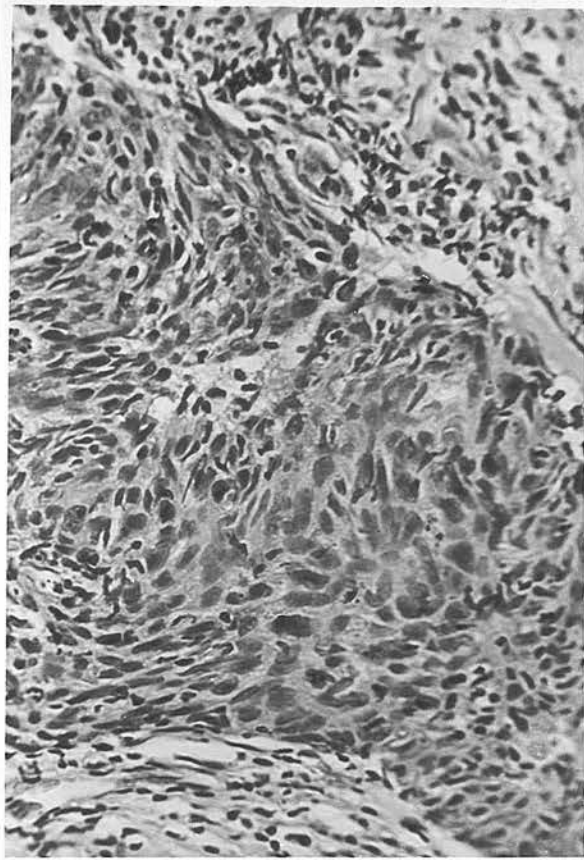


79. Same case. Anaplastic area. X 300.

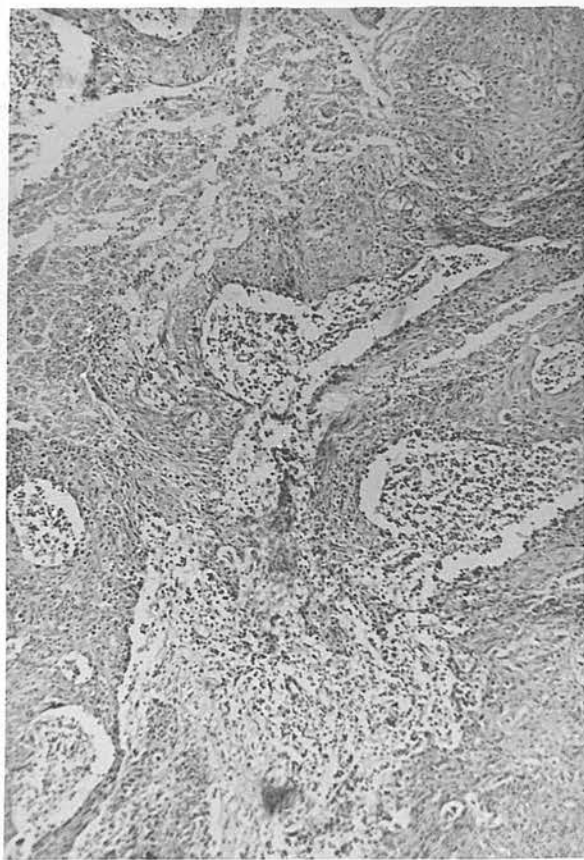


80. Irregular masses of epithelial cells. X 50.  
(case 19).

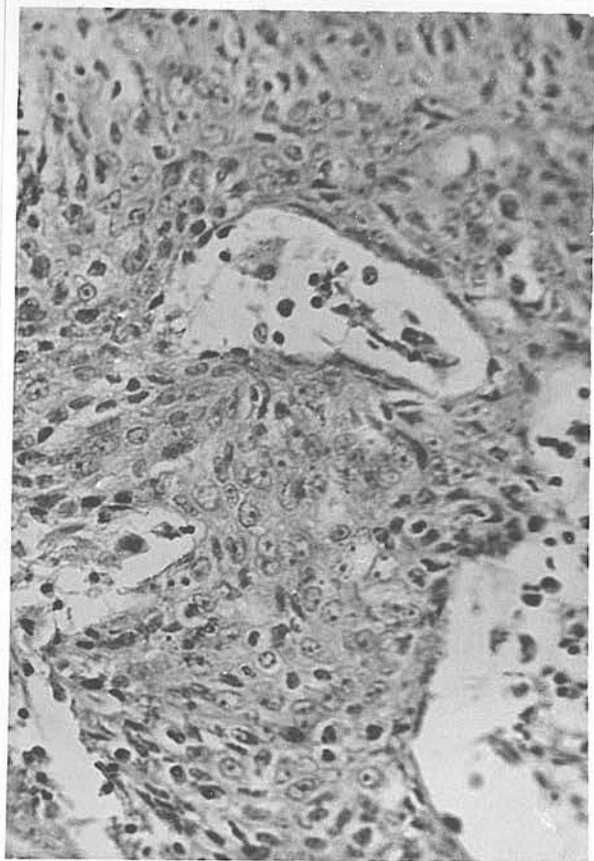




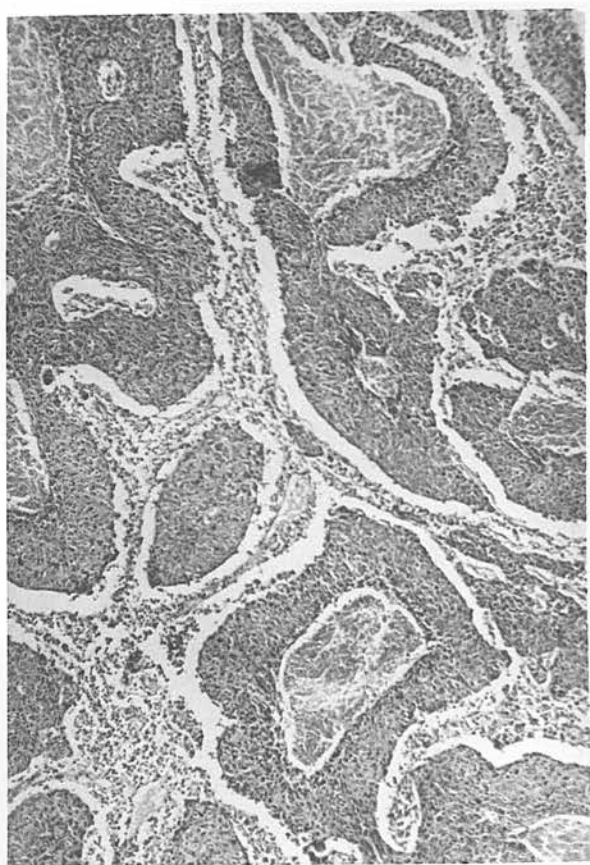
81. Same case X 300. Nuclei fairly well staining  
some prickly cells towards centre on left.



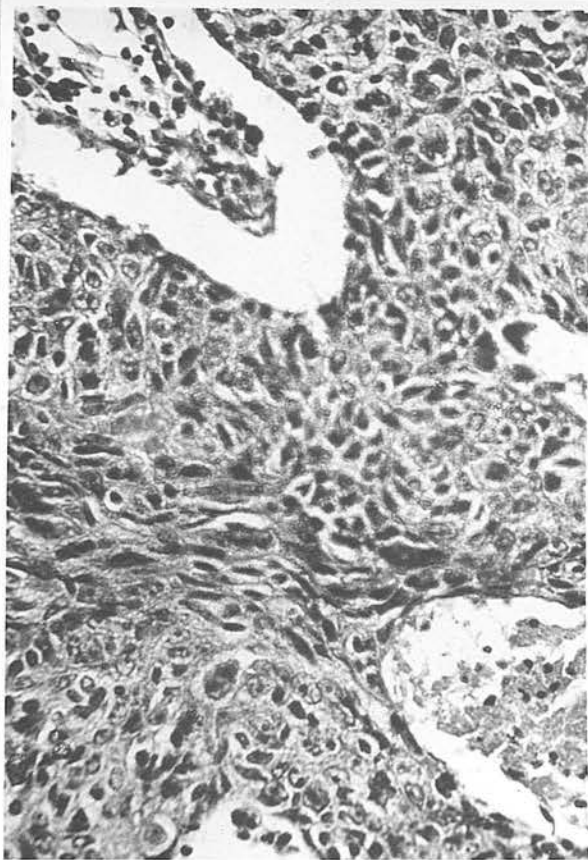
82. Lymph node metastasis of the same. X 50.



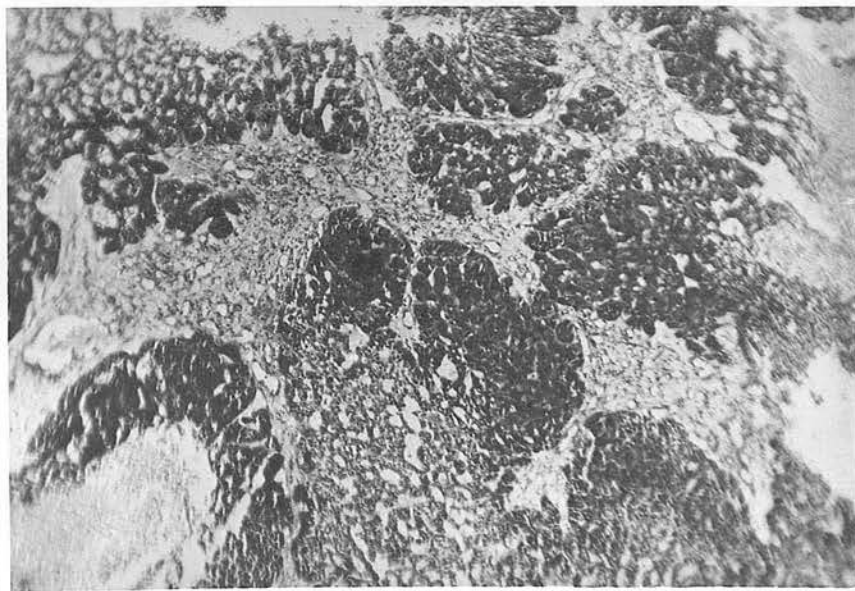
83. Lymph node metastasis X 300. Less differentiated than primary.



84. Cerebro-pontine metastasis of the same. X 50.

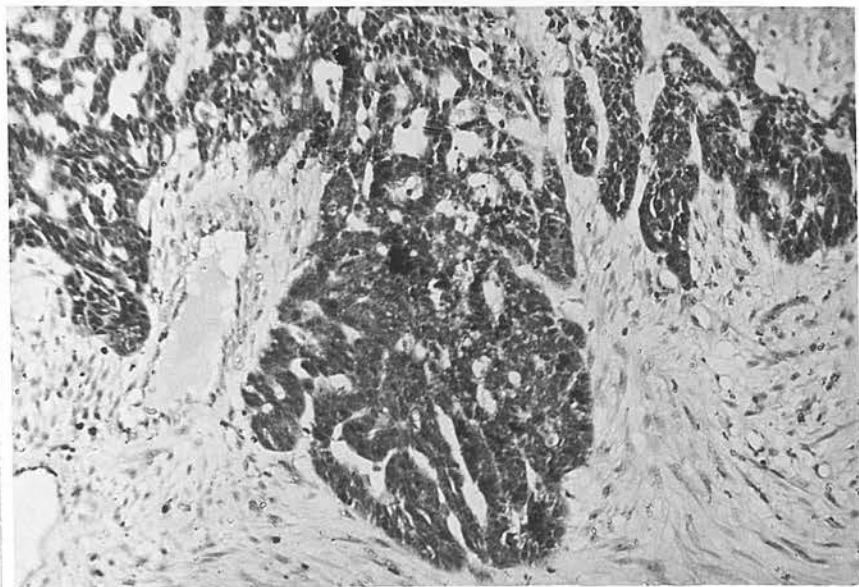


85. The same. X 300.

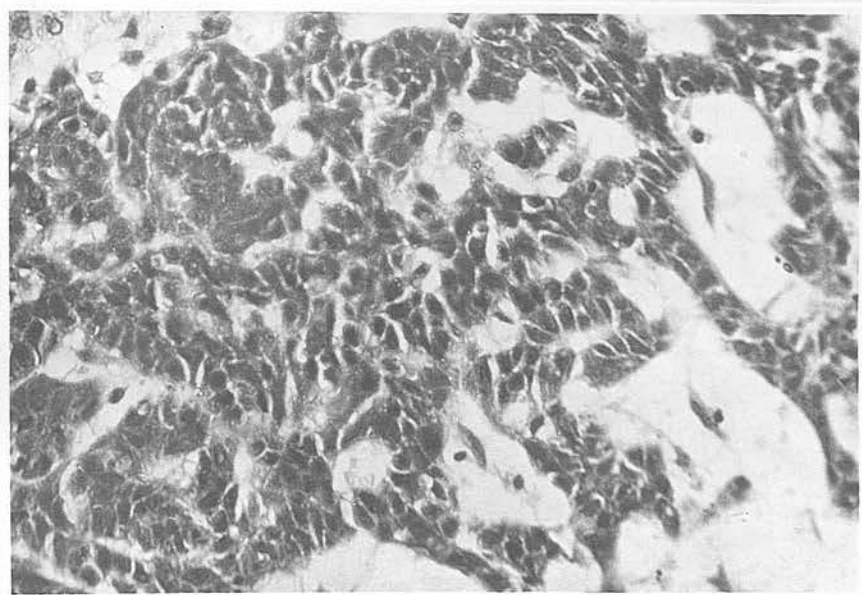


86. Tumour resembling adenocarcinoma. X 50.(case 86).

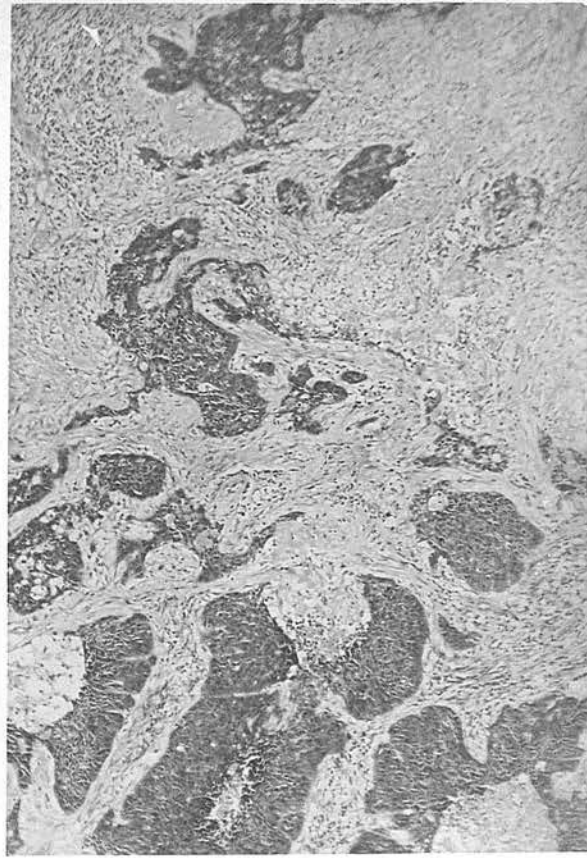




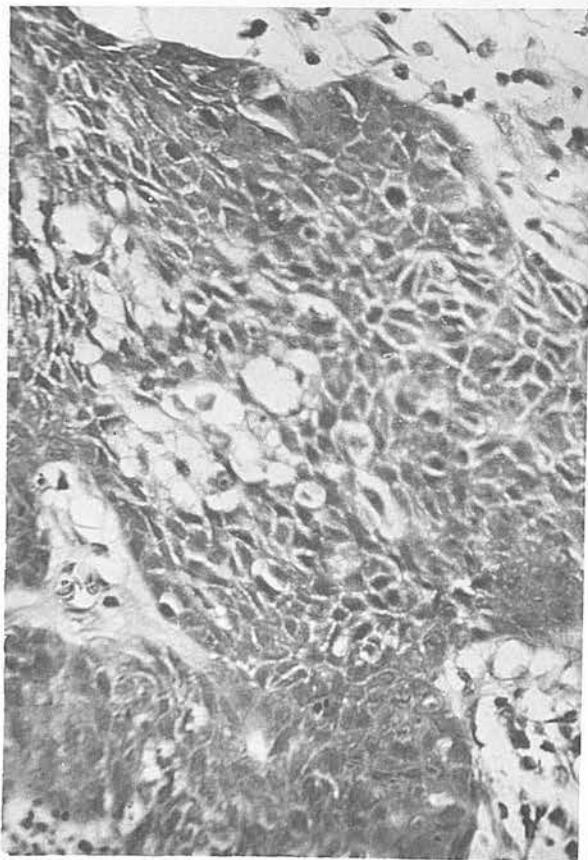
87. Closer inspection reveals squamous character.  
X 180.



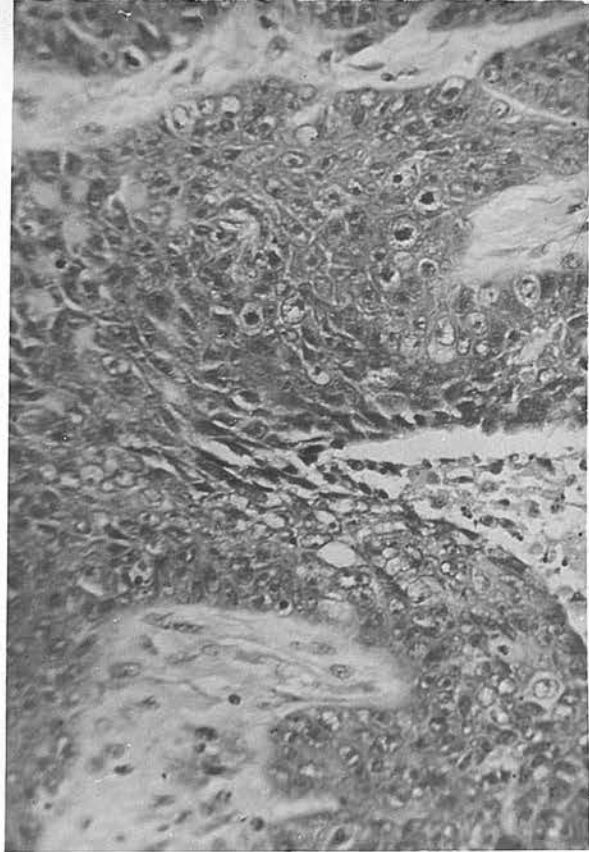
88. The same . X 300.



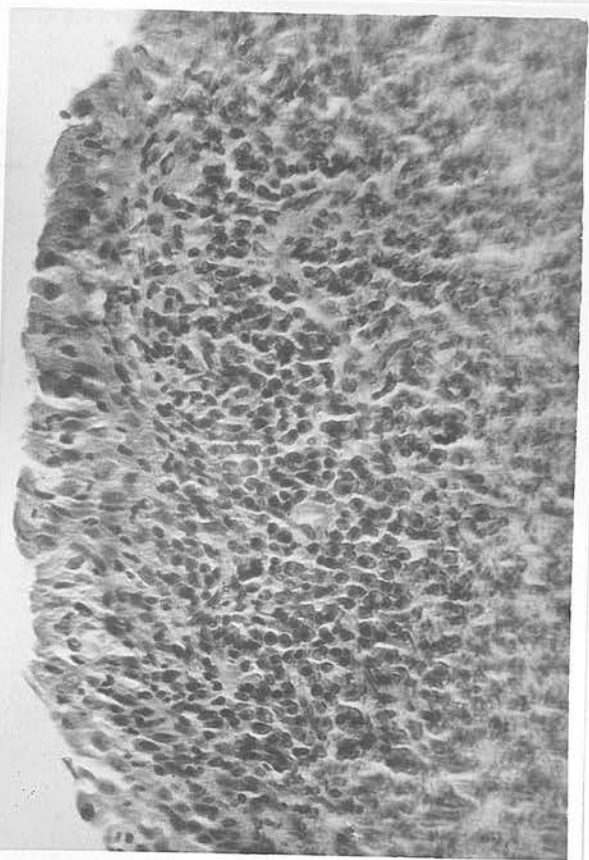
89. Lymph node metastasis of the same confirm squamous nature. X 50.



90. The same. X 300.

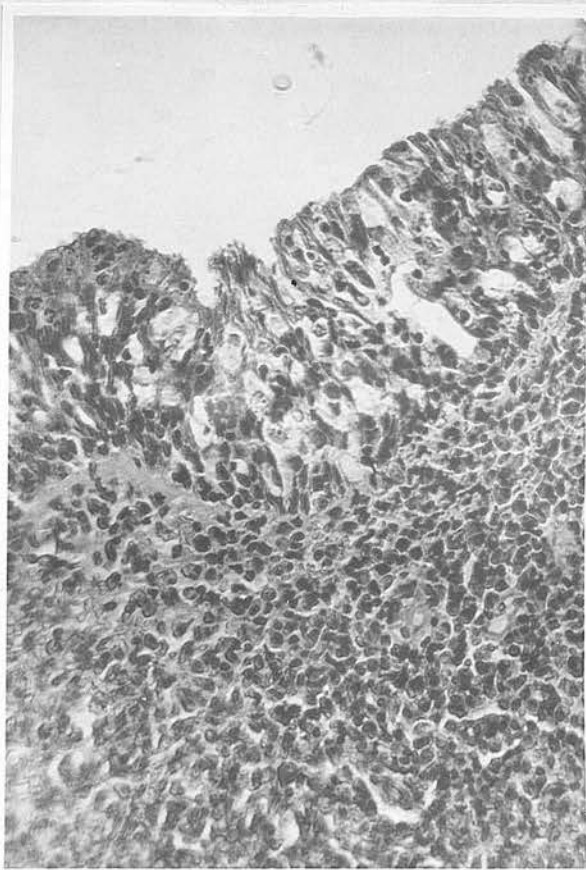


91. The same. More anaplastin area. Mitosis frequent.  
X 300.

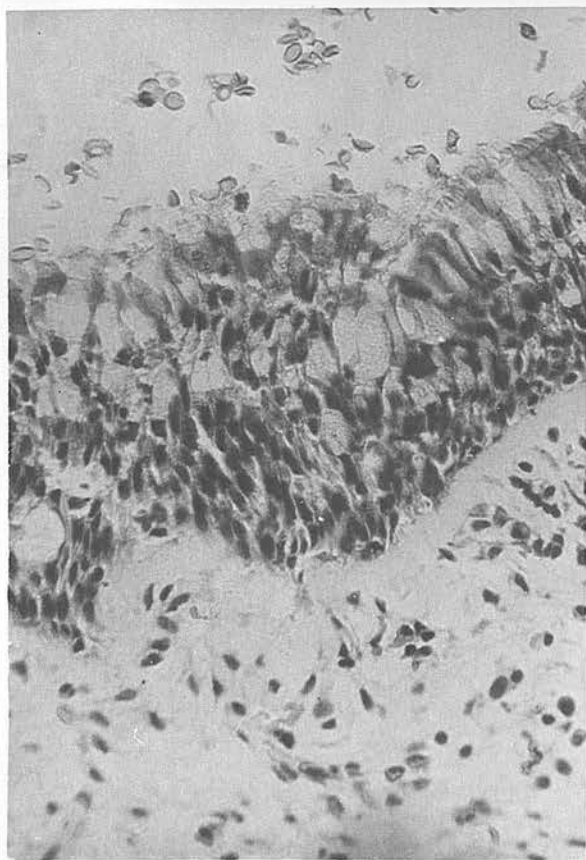


92. Transition from columnar to squamous epithelium  
in the region of a tumour. X 200. (case 47).

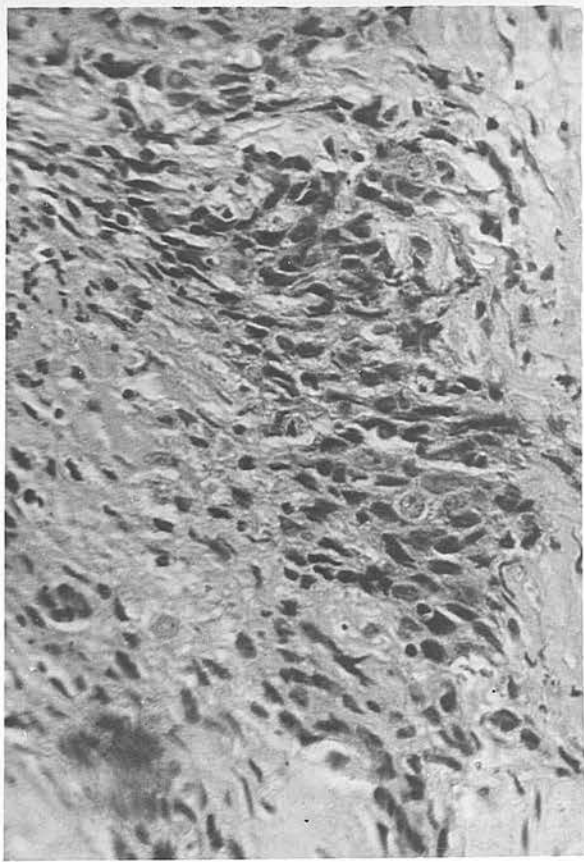




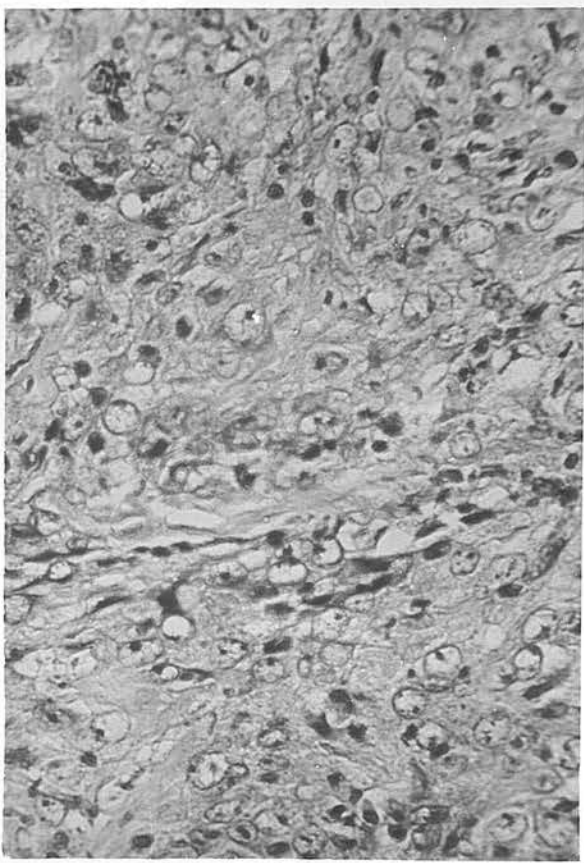
93. Same case. Columnar epithelium becoming malignant. X300.



94. Columnar epithelium becoming malignant. X 300.  
(case 89).



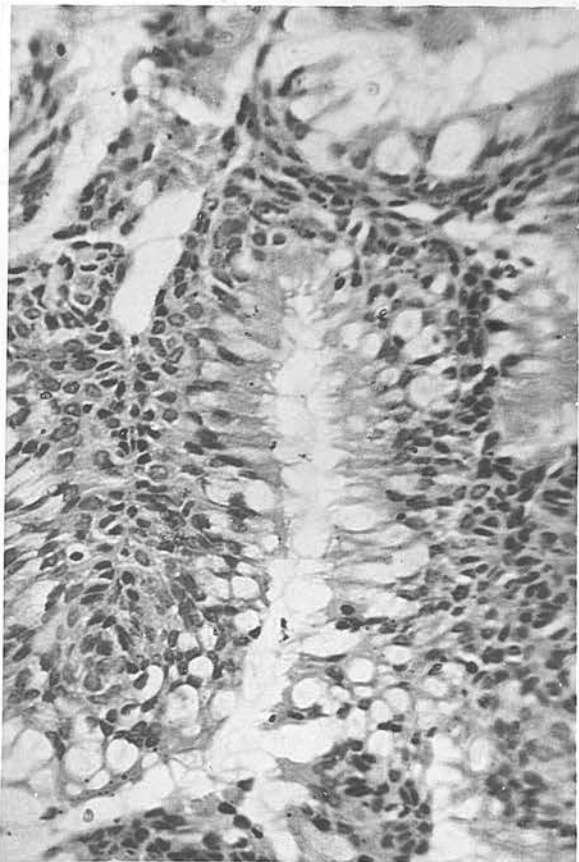
95. Part of same tumour. Cells mainly with spindle-shaped dark staining nuclei. X 200.



96. A more anaplastic part of the same tumour.  
X 300.

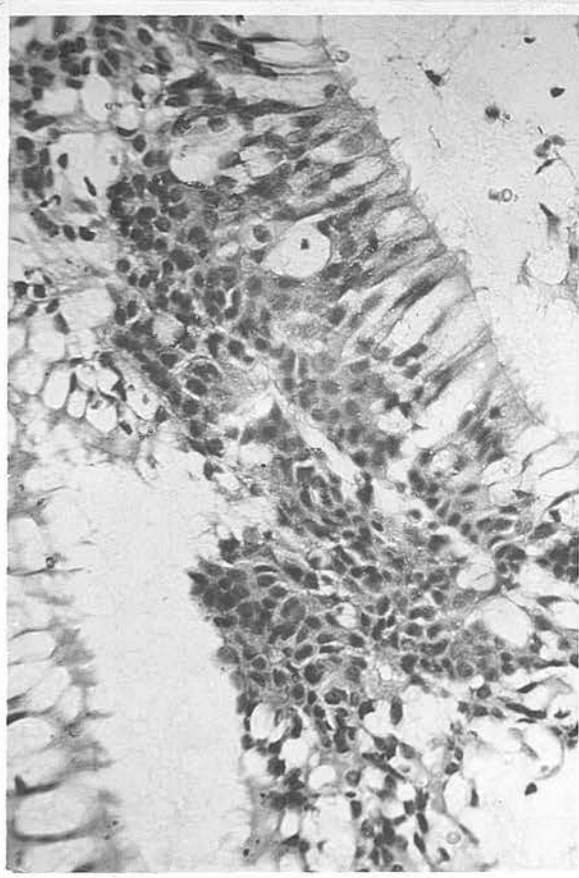


97. Transitional cell carcinoma arising from columnar epithelium. X 100.

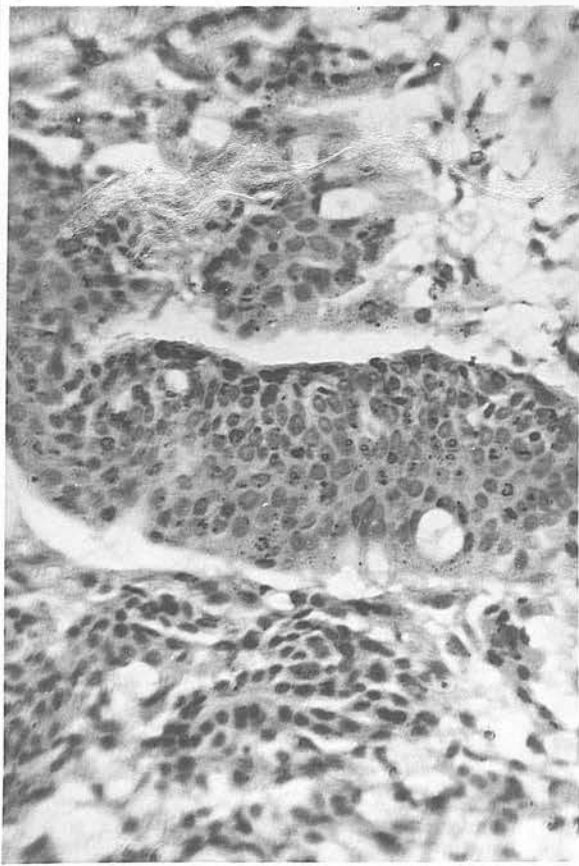


98. The same. X 300.

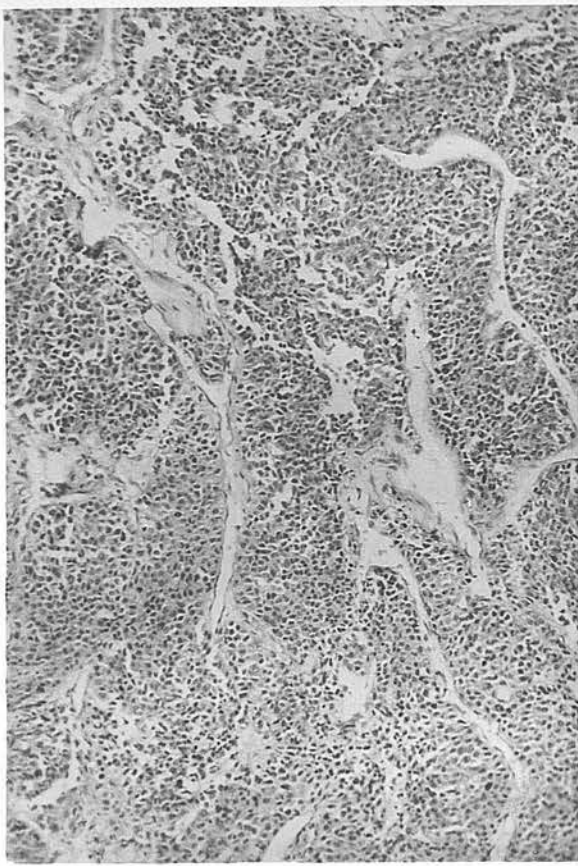




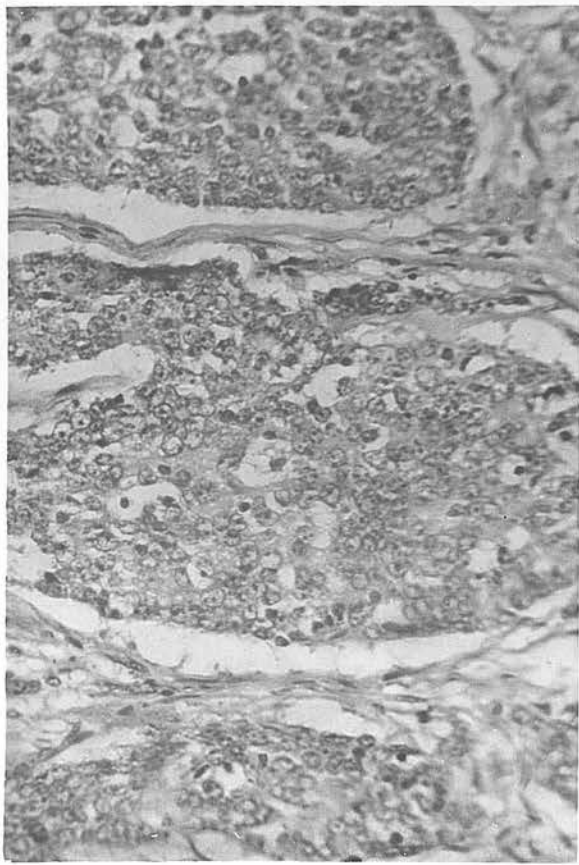
99. The same. X 300.



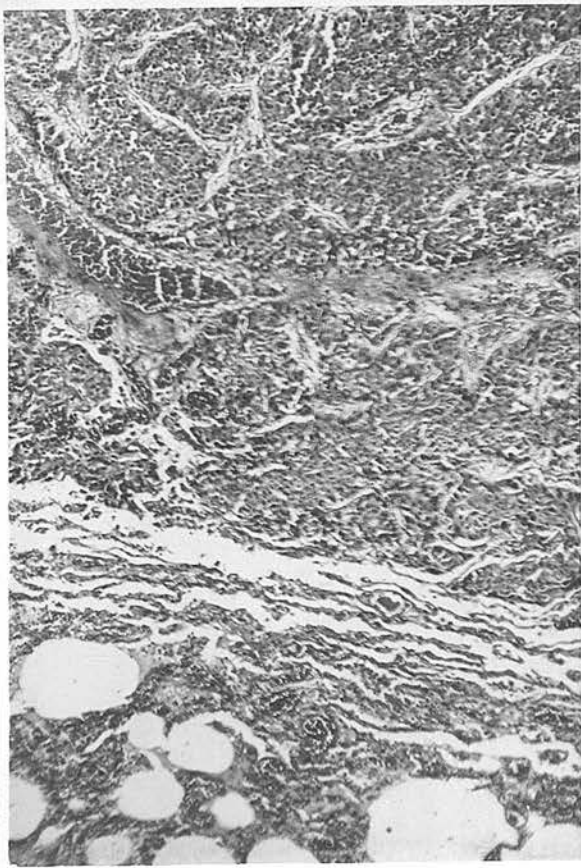
100. Part of the tumour of same. X 300.



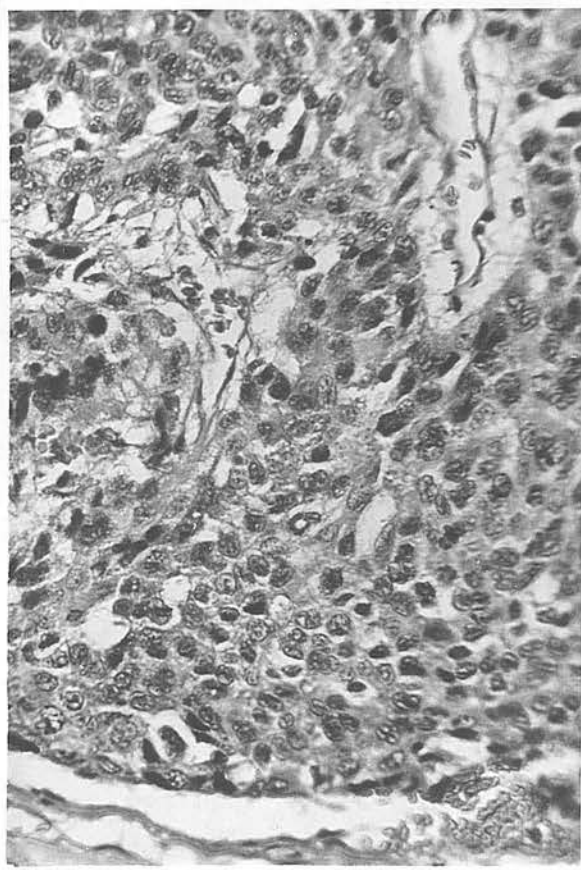
101. Lymph node metastasis of the same tumour. X 50.



102. The same. X 300.



I03. Lung metastasis of the same. X 50.

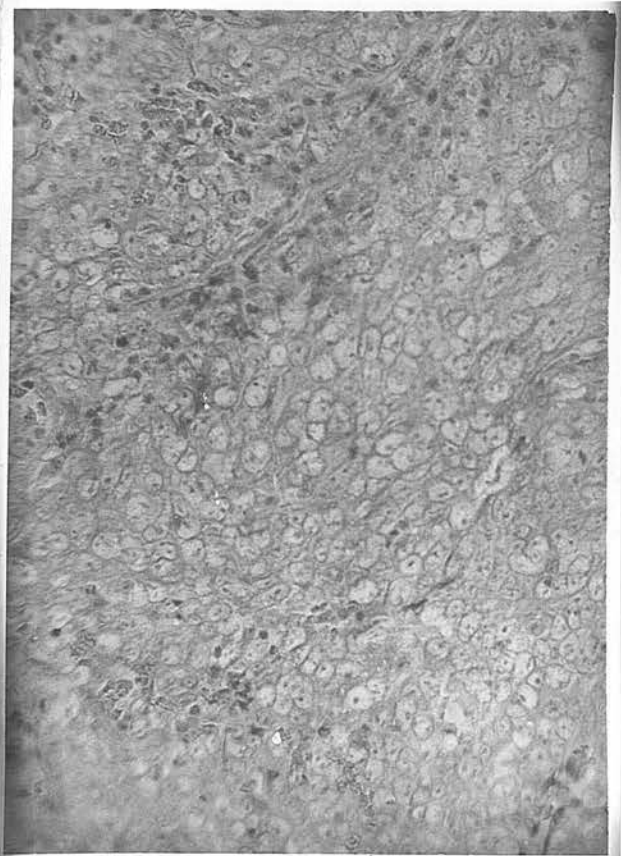


I04. The same. X 300.

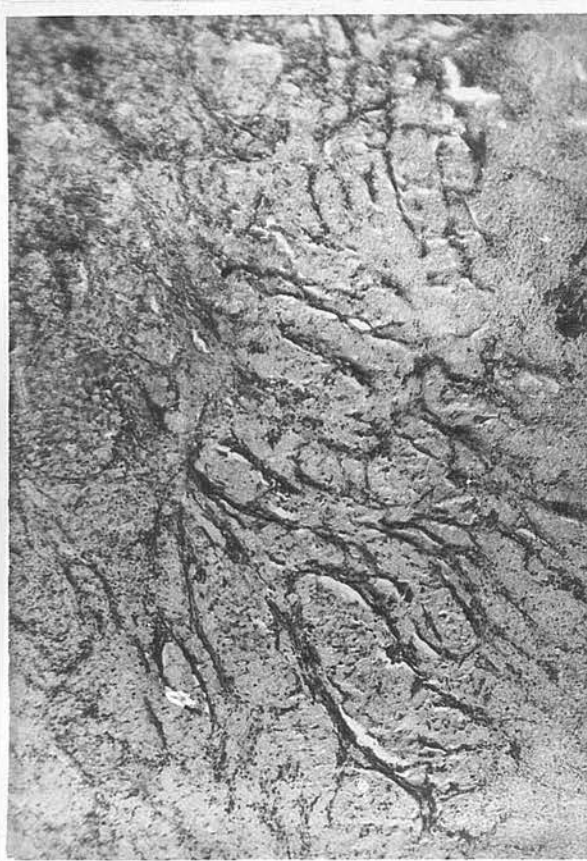




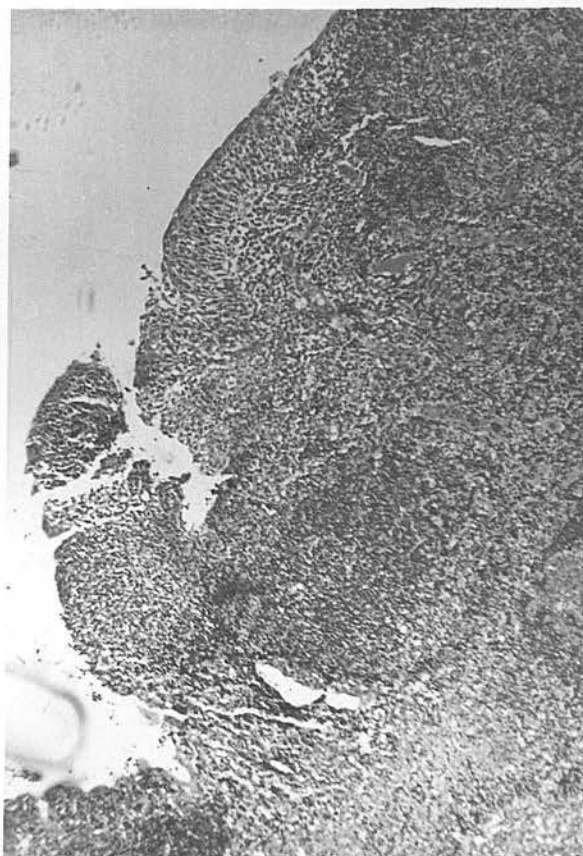
105. Anaplastic Carcinoma. X 50.



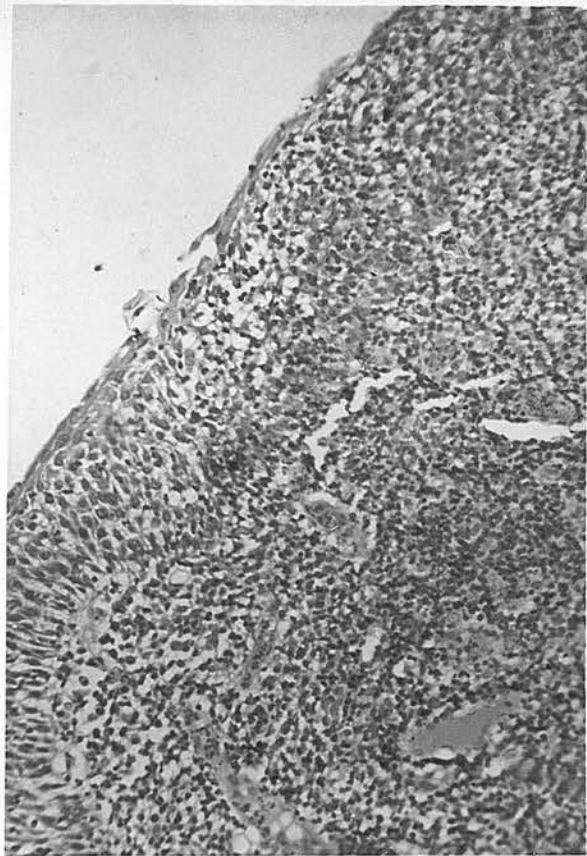
106. The same. X 300. Cords of cells packed close together reveal epithelial nature.



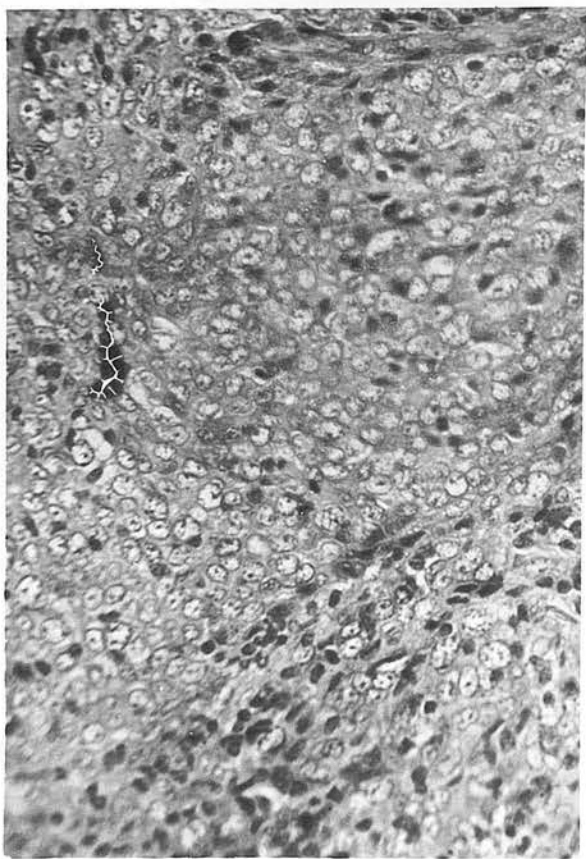
107. Reticulin staining of the same tumour emphasises its epithelial nature.



108. Lymphoepithelioma. Epithelium infiltrated with lymphocytes. X 50. (case 80).



109. The same. X 180.

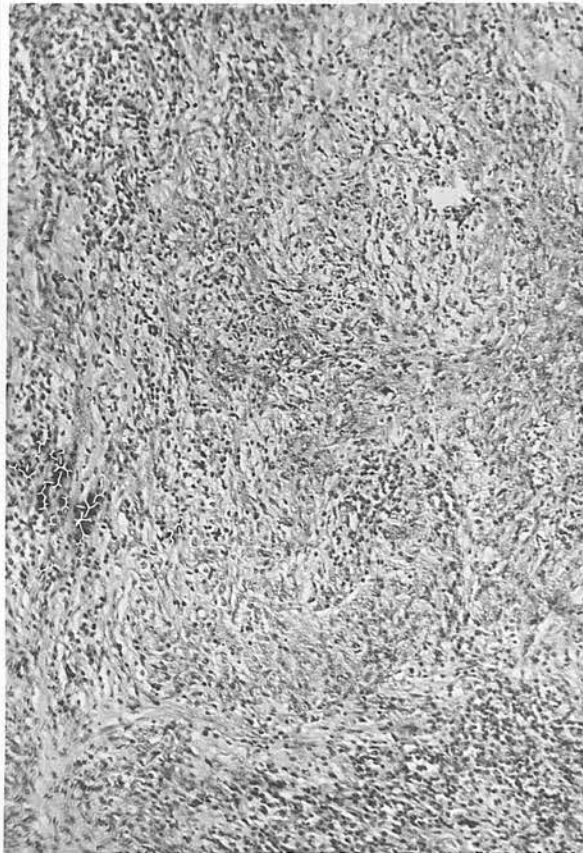


110. The same. X 300.

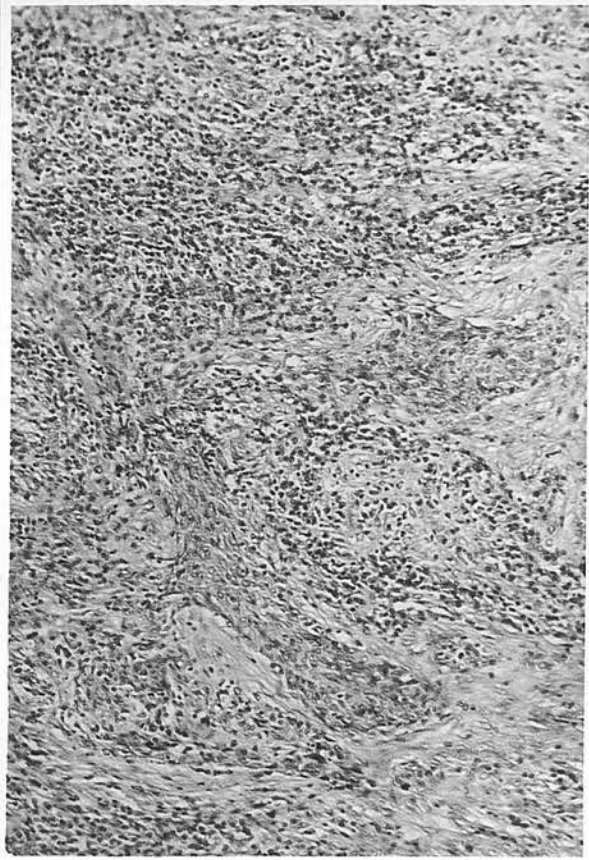




III. Lymph node metastasis revealed squamous nature. X 50.



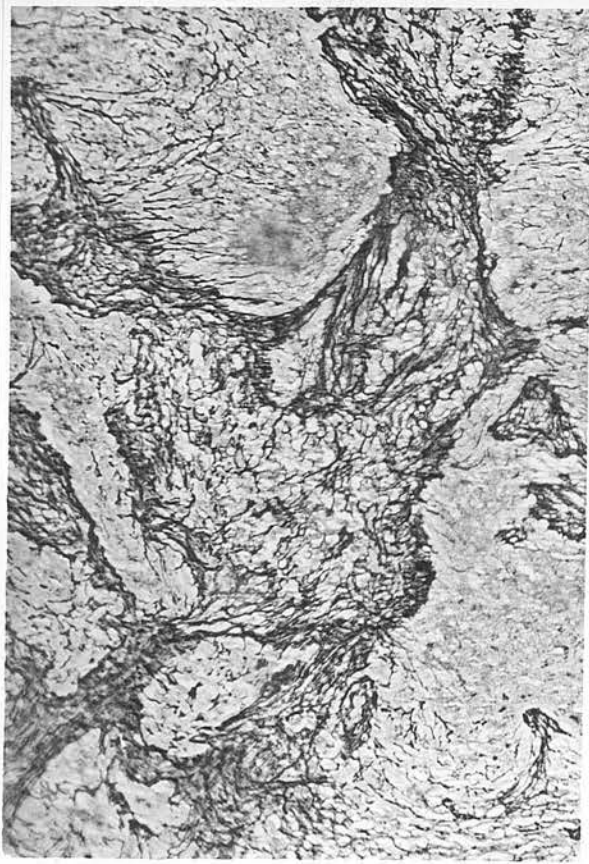
II2. Lymphoepithelioma. X 100. Very anaplastic. Resembles sarcoma. ( case 51).



II3. Same slide showing mass of epithelial cells  
in lower part. X 100.



II4. The same tumour. X 300.

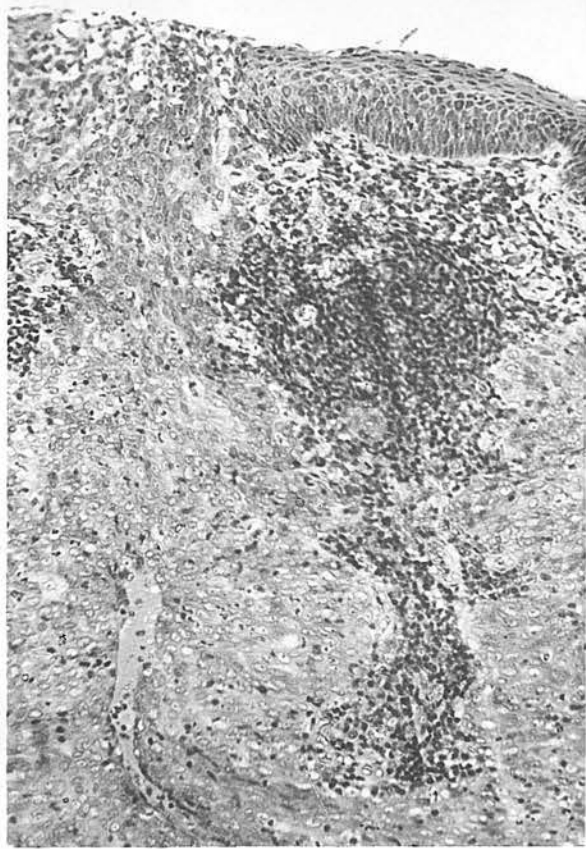


II5. Reticulum stain of the same emphasising carcinomatous nature. X 100.

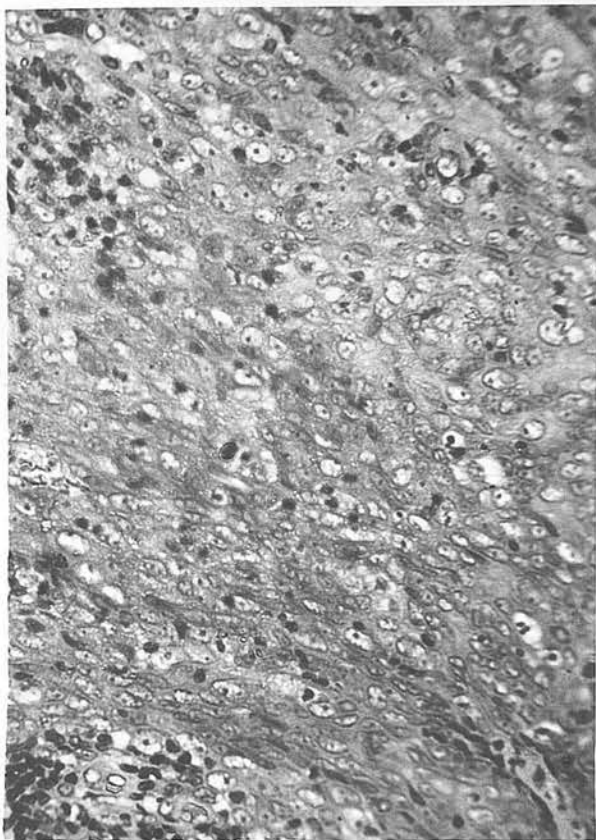


II6. Lymphoepithelioma. Epithelium infiltrated by lymphocytes. X 100. (case 44).

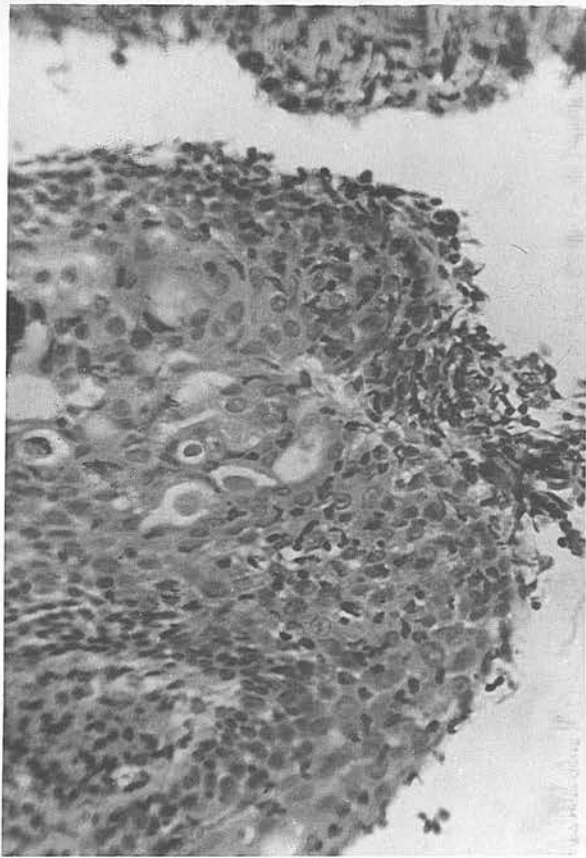




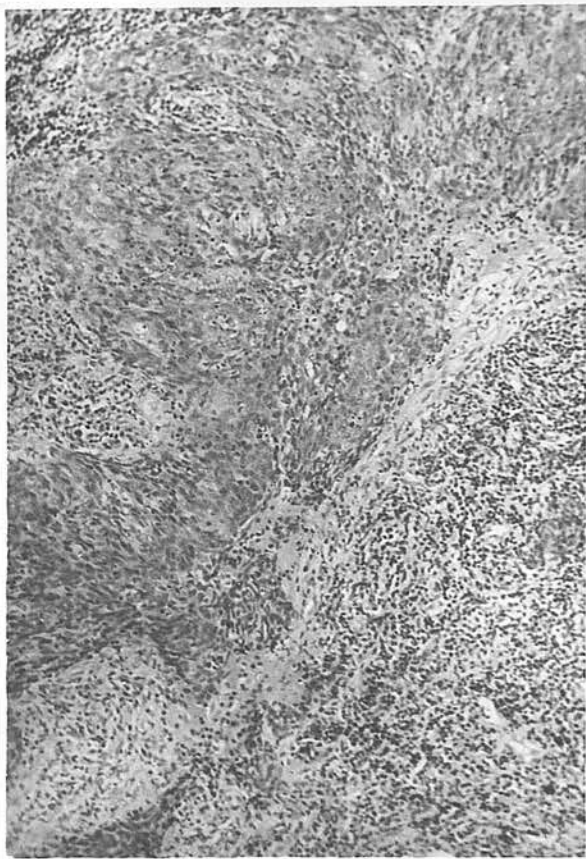
II7. The same tumour. X 180. Epithelium overlying lymphoid tissue on right. Exfoliating carcinoma on left.



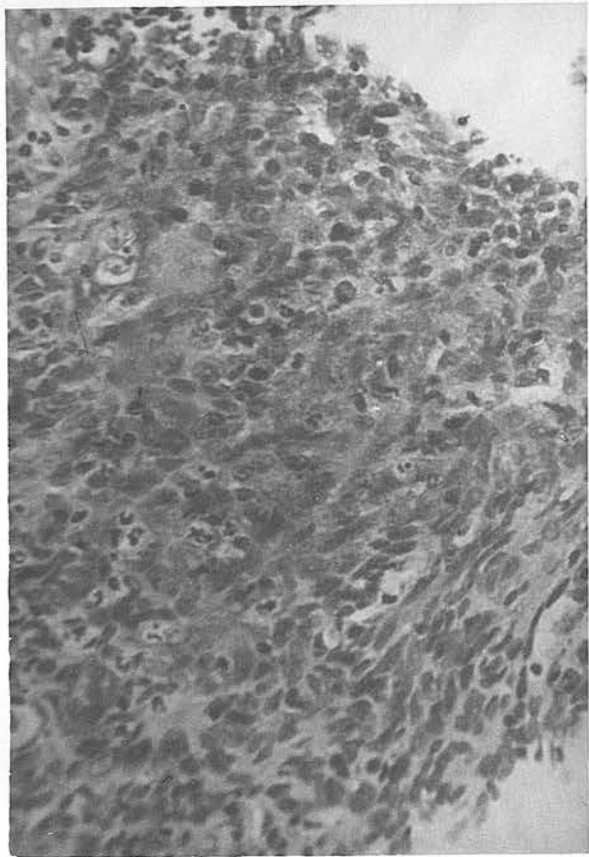
II8. Same tumour. X 300.



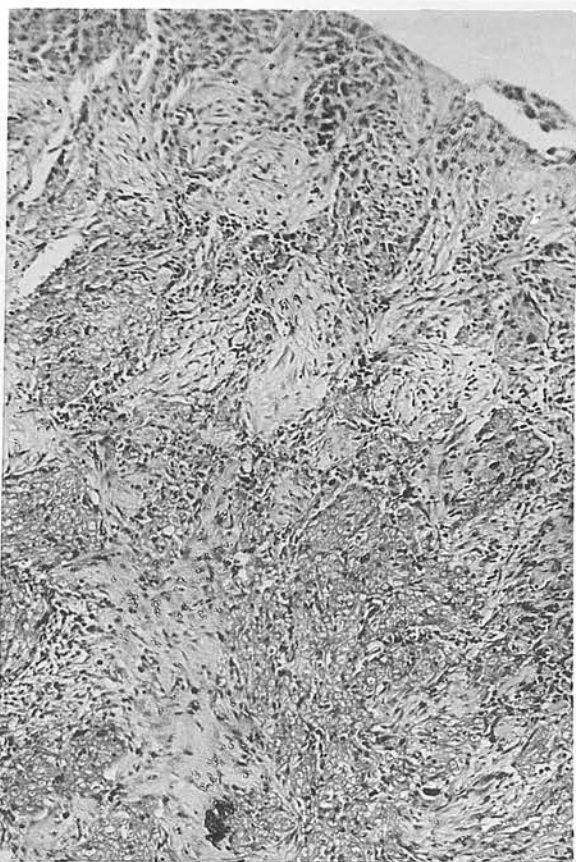
119. Same tumour. Slightly better differentiated part. X 300.



120. The same tumour after radiotherapr. Tumour more compact. X 100.

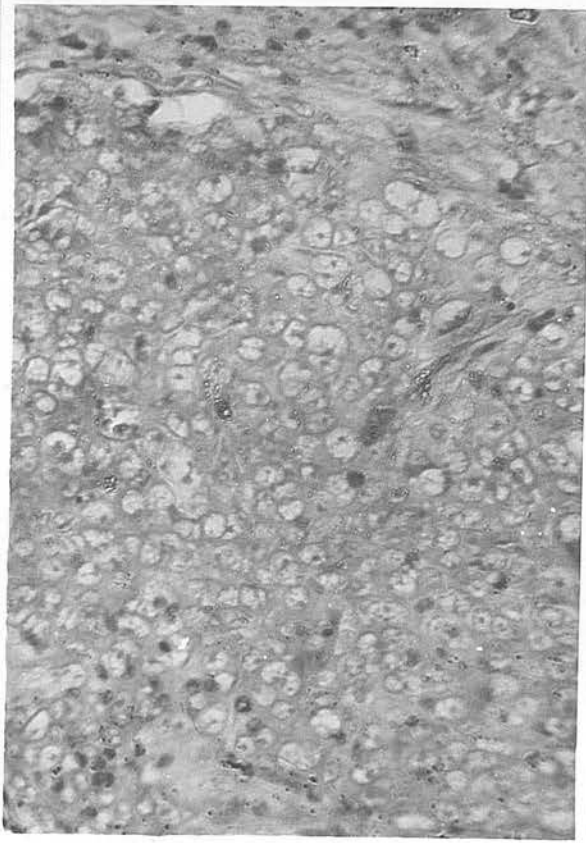


121. The same. X 300.

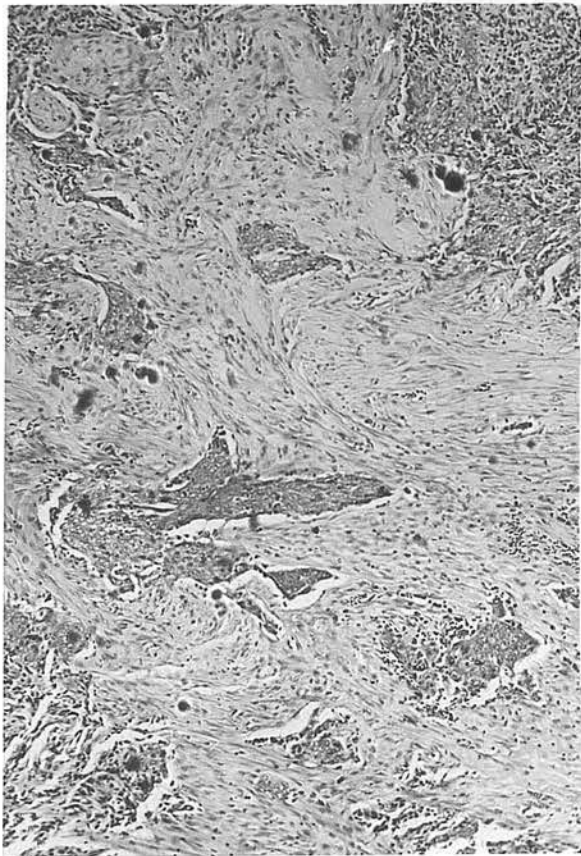


122. Anaplastic carcinoma before urethane. X50.  
(case 29).

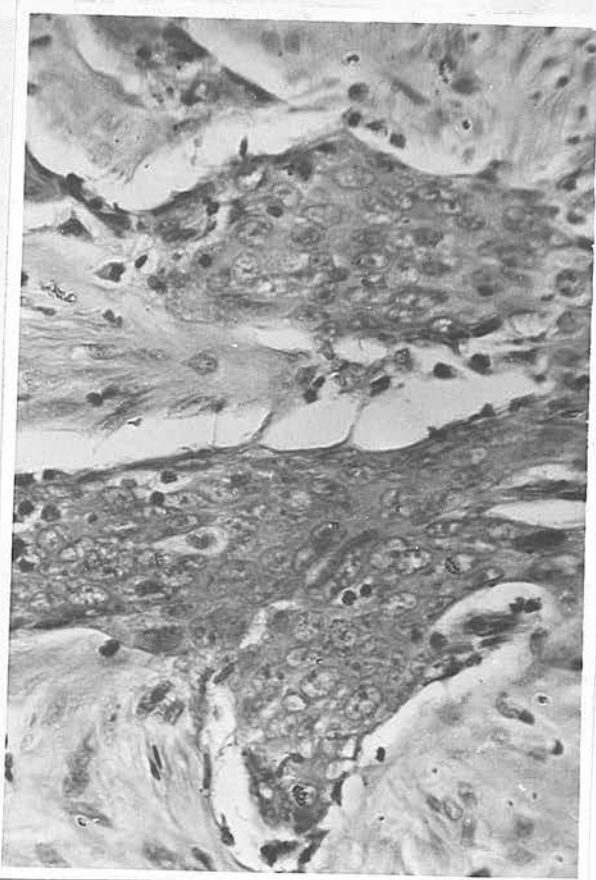




I23. The same. X 300.



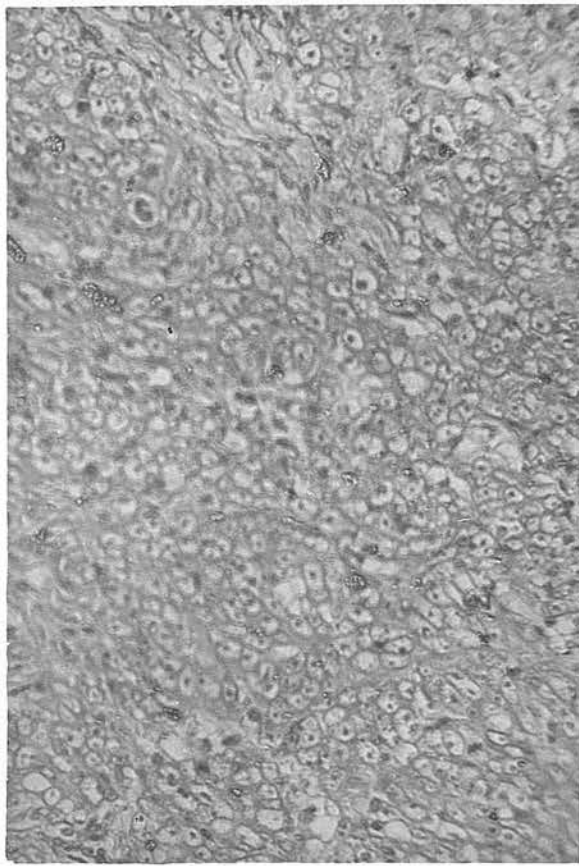
I24. Same tumour after urethane. Cells more compact.  
Stroma denser. x 50



I25. The same. X 300.



I26. Lymphoepithelioma before urethane. X 100.  
(previous case)

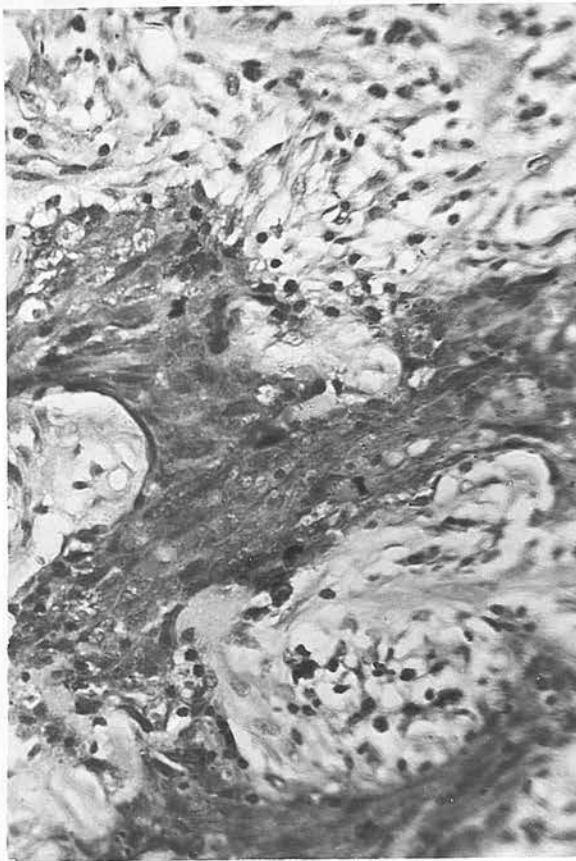


I27. The same. X 300.



I28. Same tumour after urethane. Better differentiation of tumour masses. X 50.

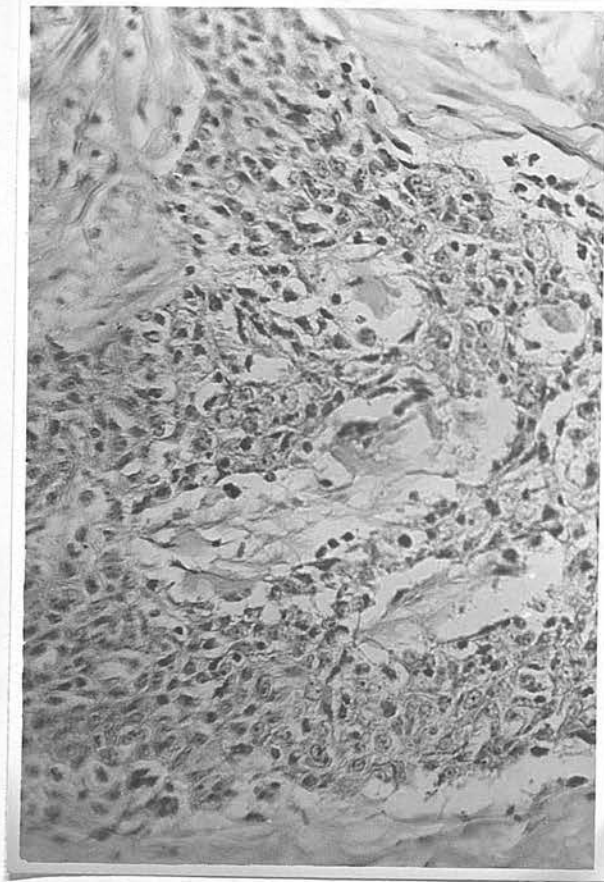




I29. The same. X 300.



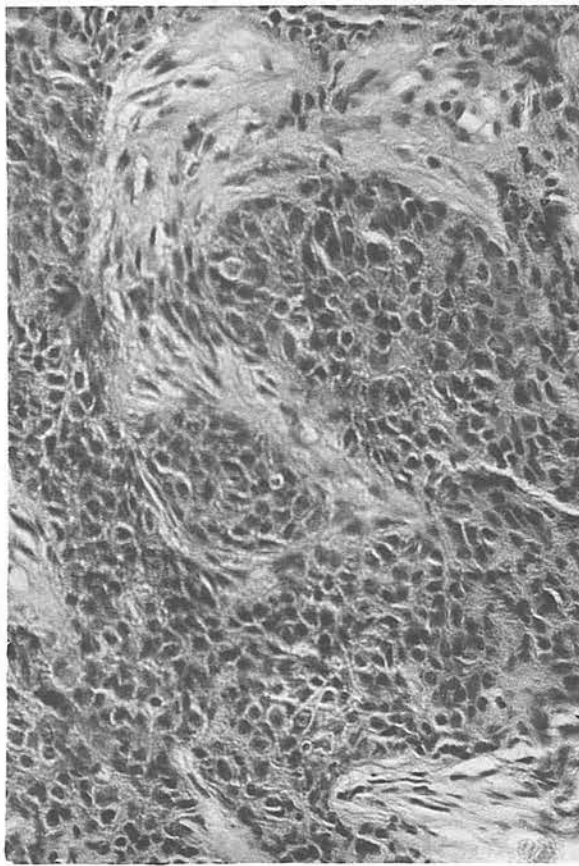
I30. Lymphoepithelioma before urethane. X 50.  
(previous case).



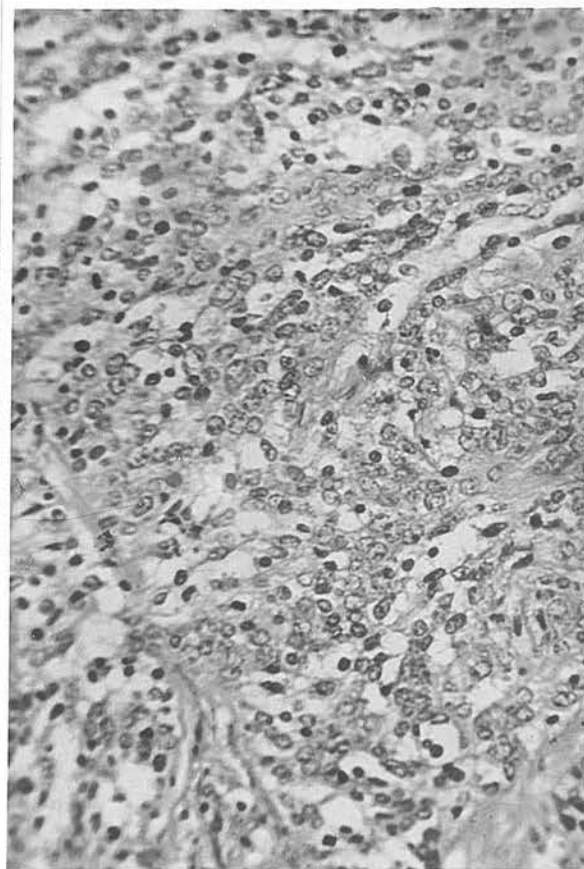
I31. The same. X 300.



I32. The same tumour after urethane. Showing squamous character. X 50.



I33. The same. X 200.



I34. Bone metastasis of the same at post mortem. Very anaplastic with frequent mitotic figures. X 300.



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APPENDIX OF CASE SUMMARIES.

Unless squamous epithelioma is described  
as differentiated, it denotes a  
Group II lesion.

Case 1. Chinese Hokien Male age 32.

History 6 months headache. 5 months bilateral cervical glands, 4 months deafness. 2 months haemoptysis. O.E. Bilateral small lymph nodes below and behind angle of jaw. Palatal paresis on left. Small white raised tumour arising from posterior wall on left. Histology lymphoepithelioma. Treated urethane and T.E.M. No response. Died 14 months from onset.

Case 2. Chinese Hainanese Male age 60.

Twelve months history of cervical swelling on left. Two months right sided neck glands, epistaxis, nasal obstruction, deafness and temporal headache on right. O.E. Moderate bilateral adenopathy, fungating tumour arising from and extending down lateral wall, on right. Erosion middle cranial fossa and second cervical vertebra. Palatal paresis. Histologically transitional cell carcinoma. Absconded. Nine months later returned with dysphagia. Absconded again. Progress unknown.

Case 3. Chinese Teochew Male age 49.

Twelve months history swelling right neck. Six

months temporal headache. Two months blurred vision and diplopia. O.E. Gross adenopathy on right, large tumour arising from and extending length of lateral wall. Erosion mid cranial fossa. Histology anaplastic carcinoma. Became very dyspnoeic and cyanosed, then died one week after presentation. Post mortem reported under Pathological features.

Case 4. Chinese Cantonese Male age 37.

History: 6 months epistaxis. 5 months temporal headache, deafness, numb left cheek, diplopia. Four months inability to chew. 3 months swelling right side neck, 1 week's swelling left side. O.E. Moderate bilateral cervical adenopathy. Fungating tumour right lateral wall of nasopharynx. Lesions right V (motor, 1st and 2nd divisions) VI. Erosion middle cranial fossa. Histology undifferentiated squamous cell carcinoma. Treated with urethane. Glands and primary diminished in size. Recurred 2 months along with lesion of left maxillary nerve, and blurred vision left eye. Two months later right facial weakness. 5 months later right ptosis. Blind R. eye. Died 2 months later, 17 months from onset.

Case 5. Chinese Cantonese Male age 52.

History 3 years epistaxis and nasal obstruction. Six months generalised headache and pain in left second



division of V. O.E. Soft friable fungating tumour of left lateral nasopharyngeal wall. Lesions left III and maxillary. Erosion middle cranial fossa. Treated urethane. No result. Progress unknown. Histology: squamous epithelioma undifferentiated.

Case 6. Chinese Hainanese Male age 48.

Three years history right sided neck glands enlarged. 9 months epistaxis, nasal obstruction, ptosis, squint and diplopia. O.E. Moderate right cervical adenopathy. Nasopharynx: hard nodular tumour from right lateral wall. Lesions right II, III, V, VI, VII and XII. Erosion middle cranial fossa. Histology: undifferentiated squamous cell carcinoma. Treated urethane. T.E.M. No response. Died 8 months later, 44 months from onset.

Case 7. Chinese Hokien Male age 32.

One month history facial asymmetry, dysphagia and dysarthria. Three weeks swelling left neck. Bitemporal and occipital headache. O.E. Moderate left cervical adenopathy. Nasopharynx huge soft friable tumour from left lateral wall. Cranial deposit over occiput. Trismus. Left palatal paresis. Lesions left III, V (motor) VII, XI and XII. Erosion middle cranial fossa. X-Ray chest pulmonary metastases. Histology: transitional cell



carcinoma. Treated urethane. No response. Died one month after presentation. Post mortem reported.

Case 8. Chinese Hainanese Male age 44.

History 2 years bilateral neck swellings. Three months nasal obstruction. Two months shooting pain right side head and ear. One month blurred vision and dysphagia. O.E. Large bilateral cervical glands. Hard nodular tumour arising from centre of posterior nasopharyngeal wall. Hard mass over upper end of sternum. X-Ray erosion of sternum. Histology: anaplastic carcinoma. Treated urethane no result. T.E.M. Sternal metastasis decreased. Progress 4 months later weakness of legs. Further progress unknown.

Case 9. Chinese Hokien Male age 47.

One month headache, earache, numb left cheek. Three weeks tinnitus. Two weeks nasal obstruction. O.E. Small glands behind left angle of jaw. Tympanic membrane bulging and opaque. Left palatal paresis. Left hemianaesthesia of face. X-Ray soft tissue swelling nasopharynx. Histology: squamous cell carcinoma. Six months later dysphagia aural discharge. Nasopharynx large growth arising from left lateral wall. Palate depressed and paralysed. Left corneal reflex absent. Progress unknown.

Case 10. Chinese Cantonese Male age 44.

2½ years swelling left neck. 6 months deafness, tinnitus, nasal obstruction and anosmia. One month swelling right neck, temporal headache. O.E. Large bilateral cervical adenopathy. Nasopharynx. Firm fungating tumour left lateral wall. Tympanic membrane opaque. Drum head retracted. Palpable glands left axilla. Wasting left sternomastoid and trapezius. Erosion middle cranial fossa. Swelling in nasopharynx on X-Ray. Histology: lymphoepithelioma. Treated urethane. No response. Died 3 months after presentation.

Case 11. Chinese Cantonese Male age 42.

3½ months headache, blurred vision, proptosis. O.E. Emaciated. Marked trismus. Lesions right II, III (absent pupillary reflexes) V (motor). Absent corneal reflex. Palpable glands right axilla. X-Ray. Sphenoid sinus invaded. Pituitary fossa enlarged and eroded. Histology: squamous epithelioma. Treated prefrontal leucotomy. Died next day. Post mortem showed indurated tumour right nasopharyngeal wall.

Case 12. Chinese Hokien Male age 38.

18 months history pain left side head and face. 12 months swelling left neck. 8 months tinnitus.



O.E. Emaciated. Small left cervical glands. Soft friable tumour centre of posterior nasopharyngeal wall. Trismus. Lesions left V motor and second divisions. Histology: squamous epithelioma. Died 2 weeks after presentation.

Case 13. Chinese Hokien Female age 40.

18 months left neck swelling and headache.

O.E. Moderate bilateral cervical glands. Nasopharynx roughening centre of posterior wall. Left palatal paresis and ptosis. Erosion mid cranial fossa. Metastasis in vault. Histology: squamous epithelioma. Treated prefrontal leucotomy. Pain improved. Deteriorated generally. Incontinent. Returned regularly for 4 months. Presumed dead.

Case 14. Chinese Cantonese Male age 46.

History 10 months nasal obstruction, epistaxis, deafness and blocking right ear. 5 months dysphagia.

O.E. Moderate right cervical adenopathy. Nasopharynx ulcer right lateral wall. X-Ray thickening posterior nasopharyngeal wall. Histology: transitional cell carcinoma. Treated X-Rays. Good response. Progress. Alive and symptom free 24 months from onset.

Case 15. Chinese Cantonese Male age 36.

History 3 years swelling left neck. 2 years



previously glands removed - recurred at once. One year right neck glands. 2 years deafness, tinnitus and aural discharge. 6 months epistaxis, nasal obstruction and anosmia. One month dysphagia. 5 days blurred vision and diplopia. One year cough and haemophysis. O.E. Bilateral small cervical glands. Nasopharynx: fungating tumour left lateral wall. Tympanic membrane perforated, serous discharge. Enlarged axillary glands. X-Ray invasion sphenoid sinus. Histology: squamous epithelioma. Treated X-Rays. Good response. 16 months later metastases in lungs and ribs. Presumed dead.

Case 16. Chinese Cantonese female age 47.

History 4 months nasal obstruction, epistaxis and deafness. One month frontal headache, pain all right side face. 2 weeks cough, haemoptysis and dyspnoea. O.E. Bilateral small cervical glands. Nasopharynx: fungating tumour of roof protruding down nose. Palatal paresis. Tympanic membrane opaque with retracted drum head. Palpable axillary glands. Numb maxillary distribution. Erosion mid cranial fossa. Histology: squamous epithelioma. Treated urethane. No result. Died 11 months from onset.

Case 17. Chinese Hokien Male age 50.

History 1 month nasal obstruction, epistaxis and

anosmia. 3 weeks bilateral neck swelling and right deafness. O.E. Moderate bilateral cervical adenopathy. X-Ray thickened posterior nasopharyngeal wall. Metastases in vault. Histology: differentiated squamous epithelioma. 3 months later tinnitus. Multiple metastases in ribs. Not seen again.

Case 18. Chinese Teochew Male age 42.

History 6 months left cervical swelling, blurred vision. 2 weeks lumbar pain. O.E. Large left cervical glands. X-Ray invasion sphenoid sinus. Histology: anaplastic carcinoma.. Treated urethane. Glands decreased. Histology: more differentiated. Glands recurred one month. Radiotherapy: glands went. 2 weeks later metastases in ribs and pelvis. Died 11 months from onset.

Case 19. Chinese Hakka Male age 37. 2 years history of epistaxis. One year nasal obstruction, temporal headache, deafness, pain in cheek, pain in chest all on right. 7 months swelling in mouth. 4 months squint and diplopia. O.E. Right palatal paresis. Nasopharynx. Soft friable tumour left lateral wall. Lesions right VI, 2nd division of V, VII. X-Ray swelling nasopharynx. Erosion sphenoid sinus. Histology: squamous epithelioma. Treated urethane. Toxic effects. Incomplete. T.E.M.

No response. Deteriorated. One month metastasis in femur. 6 months later blurred vision. 2 months later blind. 2 months later cough and haemoptysis. Died 34 months after onset. Post mortem reported.

Case 20. Chinese Hokien Male age 41. History 7 months blurred vision and diplopia. 6 months bilateral frontal headache. 4 months right cervical mass, left epistaxis nasal obstruction, facial paralysis, proptosis, ptosis and dysphagia. 2 weeks blind.

O.E. Nasopharynx. Soft friable tumour left lateral wall. Large right cervical mass. Palatal paresis. Lesions left II, III, IV, V, VI, VII, IX, X and XII.

X-Ray massive erosion mid cranial fossa. Histology: squamous epithelioma. Treated urethane. Glands

diminished. Recurred 4 months. One month later blurred vision right eye. Radiotherapy 2 months

later behind orbits for failing vision. Vision

improved in right eye. 6 months later keratitis

left eye. Trismus marked. One month later pain

left second division of V. Nasopharyngeal tumour enormous depressing palate, involving alveolus.

Glands larger. 3 months later tarsorrhaphy. One month later radiotherapy to neck glands. Improved.

Alveolar tumour disappeared. 3 months later pain in

sacrum and right hip. Further radiotherapy. Glands



smaller. Nasopharyngeal tumour went. 3 months later metastasis lumbar 5. 2 months later, vision failing. Metastases vault of skull. 2 months later metastases in lung. Alive with advanced disease 30 months from onset.

Case 21. Chinese Hainanese Male age 51.

History 8 months nasal obstruction, epistaxis and anosmia. 3 weeks dysphagia. O.E. Nasopharynx: soft friable mass centre of posterior wall. X-Ray swelling in nasopharynx. Histology: squamous epithelioma. Treated urethane. No response. Failed to complete radiotherapy. Progress unknown.

Case 22. Chinese Cantonese Male age 42.

History 10 months left cervical glands. One month epistaxis, nasal obstruction tinnitus and front-temporal headache. O.E. Nasopharynx: small fungating growth centre of posterior wall. Small left cervical glands. X-Ray swelling in nasopharynx. Invasion sphenoid sinus. Histology: squamous epithelioma. Treated X-Rays. Good response. Chronic psoriasis. Developed psoriatic arthritis. Progress unknown.

Case 23. Chinese Cantonese Male age 45.

History 1 year epistaxis and nasal obstruction. 4 months generalised headache. Two months bilateral deafness. O.E. Small ulcer near right Eustachian

orifice. Histology: squamous epithelioma. Treated urethane. Responded. Radiotherapy responded. 16 months later cervical glands on right. Blurred vision. 19 months lesions of right V (all divisions) VI, VII and XII. Alive with advanced disease 35 months from onset.

Case 24. Chinese Teochew Male age 38.

History 8 months headache and tinnitus. 5 months left cervical swelling, epistaxis and nasal obstruction. Four months numb left cheek. 2 months ptosis, blurred vision and ophthalmoplegia. O.E. Moderate left cervical glands. Nasopharynx. Hard nodular tumour of roof. Palatal paresis. Trismus. Proptosis. Left papilloedema, complete ophthalmoplegia. Ptosis. Hemianesthesia of face. V motor lesion. X-Ray massive erosion mid cranial fossa. Sphenoid sinus opaque. Histology: transitional cell carcinoma. Treated T.E.M. No result. Progress unknown.

Case 25. Chinese Cantonese Male age 36.

History 15 months headache. 12 months deafness and aural discharge. 8 months squint, diplopia and blurred vision. 2 months dysphagia and lumbar spine. O.E. Moderate right sided neck glands. Slight trismus. Palatal paresis. Fungating tumour left lateral nasopharyngeal wall. Ear drum perforated.

Serous discharge. Lesions of left V (all divisions) VI and XII. X-Ray. Metastasis lumbar 5. Vault of skull. Histology: squamous epithelioma. Treated X-Rays. Good result. Progress unknown.

Case 26. Chinese Hakka Male age 48.

History 2 years left swelling neck. 12 months right neck. 6 months tinnitus. 5 months generalised headache. One month diplopia. 2 weeks epistaxis. O.E. Large bilateral neck glands. Nasopharynx: warty growth of posterior wall. Palatal paresis. Lesions of VI, XI, and XII on left. Liver enlarged, hard, nodular. X-Ray thickening nasopharyngeal wall. Histology: reported from Kuala Lumpur as lympho-epithelioma. Treated T.E.M. No result. 2 months later ascites and oedema. Failed to return. Progress unknown.

Case 27. Chinese Hakka Male age 44.

History 14 months left cervical swelling. 11 months on right. 8 months inability to clench jaw. Temporal headache. 3 months epistaxis. O.E. Moderate bilateral cervical adenopathy. Nasopharynx. Nodular tumour of lateral wall. Lesions left V (motor) XI, XII. X-Ray thickening posterior nasopharyngeal wall. Erosion sacro-iliac joint and acetabulum. Histology: transitional cell carcinoma.



Treated X-Rays. One month later pain in chest.  
Dyspnoeic.. Died 15 months from onset. Post mortem reported.

Case 28. Chinese Hakka Male age 44.

History 7 months right neck glands. Deaf.  
O.E. Moderate right cervical adenopathy. Small nodule rear right Eustachian orifice. Histology: differentiated squamous epithelioma. Failed to return. Progress unknown.

Case 29. Chinese Hainanese Male age 33.

History 9 months swelling right neck. One month tinnitus and deafness. Two weeks epistaxis. O.E. Large right cervical glands. Palatal paresis. Nasopharynx: soft friable fungating growth of posterior wall. Histology: anaplastic carcinoma. Treated X-Rays. No response. Urethane responded. Tumour more differentiated. 8 months later liver enlarged. Oedema ankles. Did not return. Presumed dead.

Case 30. Chinese Teochew Female age 46.

History 8 months left neck swelling, followed immediately by headache and deafness. O.E. Moderate left cervical adenopathy. Small nodule rear Eustachian tube. Histology: squamous epithelioma. Did not return. Progress unknown.

Case 31. Chinese Hokien Male age 26.

History 6 months right neck swelling followed by epistaxis and nasal obstruction. Five months headache over occiput and vertex. O.E. Moderate bilateral cervical adenopathy - small nodule at junction of lateral wall and roof of nasopharynx. Histology: lymphoepithelioma. Treated X-Rays. Good response. Alive and well 11 months from onset.

Case 32. Chinese Cantonese Female age 56.

History 10 months swelling right neck. 4 months on left. 5 months epistaxis. 3 months nasal obstruction and temporal headache. O.E. Bilateral neck glands, large on right. Histology: transitional cell carcinoma. Treated X-Rays. Good response. 4 months later tinnitus. 3 months later recurrence of glands. Retreated with X-Rays - responded. Developed metastases dorsal spine and paraplegia. Progress unknown. Presumed dead.

Case 33. Chinese Hakka Female age 45.

History 4 years right neck swelling. 2 years deafness and tinnitus. 18 months epistaxis. One year swelling left neck. O.E. Bilateral small cervical glands. Nasopharynx: small plaque of lateral wall on right. Histology: anaplastic carcinoma. Treated X-Rays. Good response. Alive

and well 5½ years from onset.

Case 34. Chinese Hainanese Male age 43.

History 2 years swelling right neck. One year nasal obstruction. 6 months bilateral epistaxis and right deafness. 2 weeks blurred vision. O.E. Moderate right cervical adenopathy. Fungating growth from roof of nasopharynx depressing and paralysing palate. Right VI lesion. Erosion mid cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Glands went. Primary unchanged. Retreated, no response. 3 months later blind right eye. 3 months later tinnitus. One month later proptosis. One month later dysphagia. Then failed to return. Progress unknown.

Case 35. Chinese Hokien Male age 36.

History 6 months nasal obstruction and epistaxis. One month swelling left neck. Blurred vision, diplopia and dysphagia. 2 weeks generalised headache. O.E. Emaciated. Very weak indeed. Small left cervical glands. Nodular growth of nasopharyngeal vault depressing and ulcerating palate. Lesions of left III and VI. X-Ray erosion of sella turcica, thickening posterior nasopharyngeal wall. Histology: squamous epithelioma. Treated urethane. No response. 4 months later proptosis and blind left eye. Trismus



marked. Died 14 months from onset.

Case 36. Chinese Teochew Male age 53.

History 8 months epistaxis. 4 months occipital headache, deafness, and swelling right neck. 3 months diplopia and blurred vision. O.E. Moderate right cervical adenopathy. Nasopharynx: ulcer of lateral wall. Palatal paresis. Lesions left VI and right XII. X-Ray erosion mid cranial fossa. Histology: squamous epithelioma. Treated urethane toxic effects - stopped. Deteriorated. 6 months later trismus. Glands and primary larger. Lesions left II, III, VI and Horner's syndrome. Right X, XI, XII. One month later dysphagia. One month later cough and haemoptysis. Lesions right VII, IX and XI, left II, III, IV, V, VI and proptosis. Failed to return. Presumed dead.

Case 37. Chinese Hokien Male age 41.

History 2 years swelling left neck, 20 months right. 8 months low back pain. 6 months deaf. O.E. Emaciated. Moderate bilateral cervical adenopathy. Nasopharynx: hard mass arising from posterior wall. Fixed mass right iliac crest. X-Ray sphenoid sinus invaded. Erosion clavicle, D12 and sacrum. Histology: squamous spithelioma. Treated X-Rays to metastases. One month later retention of urine.

Suprapubic cystostomy. Died 3 years after onset.

Case 38. Indian Tamil Male age 57.

History 5 months swelling right neck. 3 months left neck. 2 months temporal headache and deaf.

O.E. Moderate bilateral cervical adenopathy.

Nasopharynx: fleshy tumour from right lateral wall.

X-Ray erosion mid cranial fossa. Thickened posterior nasopharyngeal wall. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive and well 23 months from onset.

Case 39. Chinese Teochew Female age 27.

History 14 months discharge left ear. 13 months swelling left neck. 10 months fronto-temporal headache. 8 months epistaxis and nasal obstruction. 6 months dysphagia. O.E. Large left cervical glands, fungating tumour from left lateral wall. Tympanic membrane perforated, purulent discharge. Histology: anaplastic carcinoma (and tuberculosis in glands).

Treated. Streptomycin: no response. X-Rays: good response. Died 26 months from onset.

Case 40. Chinese Hokien Male age 60.

History 18 months swelling left neck. 12 months cough. One month pain in ear and tinnitus. 2 weeks epistaxis, nasal obstruction, temporal headache, dysphagia, hoarseness and swelling right neck. O.E.



Emaciated. Enormous bilateral cervical glands. Palatal paresis. Laryngeal paralysis. Nasopharynx: huge mass arising from roof depressing and paralyzing palate. Lesions of left V (motor) X and XI. X-Ray huge neck mass pushing oropharynx, larynx and trachea to right. Erosion of C5. Histology: squamous epithelioma. Treated T.E.M. No result. Became increasingly dyspnoeic. Died 2 weeks after presentation.

Case 41. Chinese Hokien Female age 33.

History 6 months epistaxis. 5 months temporal headache. 6 weeks swelling right neck. O.E. Bilateral cervical adenopathy, larger on right. Nasopharynx: bulging of posterior wall. X-Ray thickening posterior nasopharyngeal wall. Histology: anaplastic carcinoma. Treated urethane - toxic effects, stopped. X-Rays. Good response. Alive and well 29 months from onset.

Case 42. Chinese Cantonese Male age 54.

History 3 months bilateral neck swellings. Cough. One month pain in ear and tinnitus. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: hard nodular mass from right lateral wall. X-Ray erosion middle cranial fossa. Thickening posterior nasopharyngeal wall. Histology: squamous epithelioma.



Treated X-Rays. Good response. Alive and well 21 months from onset.

Case 43. Chinese Teochew Male age 48.

History 6 months swelling right neck. 5 months bilateral epistaxis nasal obstruction, tinnitus and occipital headache. Diplopia, blurred vision and squint of left eye. One month swelling left neck. O.E. Bilateral small cervical glands. Palatal paresis. Left VI lesion. X-Ray erosion of sella turcica. Histology: squamous epithelioma. Primary seen 3 months later - fungating tumour right lateral wall. Treated X-Rays. Primary disappeared. Glands responded slightly. Alive 22 months from onset.

Case 44. Chinese Cantonese Male age 29.

History 2 years temporal headache. One year swelling left neck, 5 months right neck. 5 months epistaxis. 3 months deaf. O.E. Bilateral large cervical glands. Palatal paresis. Nasopharynx: large fungating growth from left lateral wall. Lesions left VI and XI. X-Ray erosion sella turcica. Histology: Lymphoepithelioma. Treated X-Rays. Good response. Glands recurred 7 months later. Primary recurred 3 months later still. Retreated. No response. Alive 30 months from onset.

Case 45. Chinese Cantonese Male age 37.

History 2 years bilateral swellings in neck, left deafness and tinnitus. One year epistaxis, nasal obstruction and temporal headache. 2 weeks diplopia and hoarseness. O.E. Bilateral gross cervical adenopathy. Trismus. Palatal paresis. Nasopharynx: fungating mass of left lateral wall. Lesions left VI and XI. X-Ray erosion sella turcica. Histology: anaplastic carcinoma. Treated urethane. Toxic effects, stopped. Radiotherapy, response slight. Developed shingles sensory distribution of C5 to C7. Retreated, no response. Alive 37 months from onset.

Case 46. Chinese Hakka Male age 44.

History one year left neck swelling. 11 months deaf. 3 days epistaxis. O.E. Moderate left cervical adenopathy. Erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 10 months later metastasis in pelvis treated with X-Rays. Alive 23 months from onset.

Case 47. Chinese Cantonese Male age 35.

History 2 months swelling left neck. One month deafness, tinnitus, blurred vision, numbness of cheek, epistaxis, nasal obstruction. 2 weeks temporal

headache. O.E. Small left cervical glands.

Nasopharynx: small hard raised patch centre of posterior wall. Lesion 2nd division of V.

Histology: squamous epithelioma. Treated X-Rays. Good response. Progress unknown.

Case 48. Chinese Hakka Female age 38.

History 7 months swelling right neck, followed by blurred vision and diplopia. 4 months swelling left neck, temporal headache and bilateral deafness and tinnitus. O.E. Bilateral small cervical glands. Large fungating tumour from nasopharyngeal vault. Tympanic membrane opaque, drum head retracted. X-Ray thickening nasopharyngeal wall. Histology: anaplastic carcinoma. Treated X-Rays. Good response. Progress unknown.

Case 49. Chinese Hakka Male age 17.

History 4 years epistaxis and nasal obstruction. 8 months swelling left neck, generalised headache and bilateral aural discharge. O.E. Bilateral small cervical glands. Nasopharynx: large fungating tumour of roof. Tympanic membrane opaque, perforated, serous discharge. X-Ray erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Excellent response. 11 months later pain right loin. Haemoglobin 38%. Bilateral cervical adenopathy.



X-Ray erosion ala of sacrum. Radiotherapy to sacrum. Became paraplegic. Died 59 months from onset.

Case 50. Chinese Teochew Male age 50. Brought in by police having collapsed in street.

History 18 months swelling right neck and epistaxis. 12 months headache, deafness, blurred vision and ptosis. Bedridden for 6 weeks. O.E. Emaciated. Trismus. Gross right cervical adenopathy. Palatal paresis. Large fungating growth arising from roof of nasopharynx. Liver enlarged, firm and nodular. Oedema. Lesion right III. X-Ray erosion pituitary fossa. Posterior clinoids eroded. Histology: anaplastic carcinoma. Deteriorated. Became very dyspneic. Died one month after presentation. Post mortem reported.

Case 51. Chinese Hainanese Female age 44.

History 2 years swelling right neck. One month frontal headache and deafness. One week blurred vision, slurred speech. O.E. Moderate right cervical adenopathy. Lesion right VI. Erosion at petrous apex. Histology: lymphoepithelioma. Treated X-Rays. Good response. 5 months later tinnitus and diplopia. 3 months later lumbar pain, metastasis L4. 5 months later metastases lung and sacro-iliac joint. Lesion V (motor). Alive 37 months from onset with advanced disease.

Case 52. Chinese Cantonese Female age 52.

Three year history of swelling right neck. One month dysphagia. O.E. Small cervical gland on right. X-Ray erosion of middle cranial fossa. Treated radiotherapy. Good response. Alive 40 months from onset.

Case 53. Chinese Teochew Female age 37.

18 months previously had been diagnosed as nasopharyngeal carcinoma but only attended a few times for radiotherapy. Returned with 3 months history of headache, deafness, blurred vision, ptosis, feeling the tongue twisted, inability to shut the mouth. 10 days dysphagia. O.E. Emaciated. Bilateral small cervical glands. Trismus. Palatal paresis. White nodular exophytic growth of left lateral wall of nasopharynx. Ear drum perforated. Serous discharge. Lesions of left III, IV, V (all divisions) VI, IX, X, XI, XII. Horner's syndrome. X-Ray erosion middle cranial fossa. Posterior clinoids eroded. Sphenoid sinus opaque. Histology: squamous epithelioma. Treated X-Rays. Gland and primary went but deteriorated steadily. Presumed dead.

Case 54. Chinese Hokien Male age 52.

History 8 months epistaxis and nasal obstruction,

followed by right neck swelling. 4 months swelling left neck. One month pain right cheek. O.E. Bilateral moderate cervical adenopathy. Nasopharynx: small white nodule of right lateral wall near Eustachian tube. Lesion right XII. X-Ray opacity of sphenoid sinus. Histology: anaplastic carcinoma. Only attended once for radiotherapy. Progress unknown.

Case 55. Chinese Hokien Male age 51.

History one year deafness. 3 months tinnitus, epistaxis and nasal obstruction. 6 weeks dysphagia and hoarseness. 2 weeks neuralgia cheek. O.E. Huge growth arising from roof and depressing and paralyzing palate. Vocal cord paresis on left. Lesions of V motor and second divisions, X and XII. X-Ray shadow in nasopharynx. Erosion of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 5 months later numb left cheek. 2 months later spastic gait. Metastases in dorsal and lumbar spines, humerus, femur and ribs. Did not return for treatment to metastases. Presumed dead.

Case 56. Chinese Hakka Male age 42.

History 6 months swelling left neck. 4 months epistaxis. O.E. Small gland left side neck. Nasopharynx: small nodule on roof posterior to choanae.



Lesions of left VI. X-Ray thickening of nasopharyngeal wall. Histology: lymphoepithelioma. Treated X-Rays. Good response. Alive 13 months from onset. Still with VI lesion.

Case 57. Chinese Hainanese Male age 49.

History 2 years swelling left neck, 4 months right neck, 2 months deafness and tinnitus. One month bilateral nasal obstruction. Severe occipital headache. 2 weeks bilateral epistaxis. O.E. Large bilateral cervical glands. Palatal paresis. Huge fungating tumour arising from right lateral nasopharyngeal wall. Enlarged axillary lymph nodes. Lesion right X and XI. X-Ray erosion of cervical vertebrae. Histology: anaplastic carcinoma. Treated. Prefrontal leucotomy. Became unmanageable but pain improved. Transferred to Mental Hospital. Later sent home. Died 30 months after onset.

Case 58. Chinese Cantonese Male age 54.

History 5 years bilateral swellings in neck. 3 times "removed" and recurred. 18 months blurred vision and diplopia. One year epistaxis and nasal obstruction. O.E. Emaciated. Large bilateral cervical glands. Palatal paresis. Nasopharynx: fungating growth of left lateral wall. Vocal cord paralysis. Axillary lymphadenopathy. Lesions of

left IX, X, XI, XII or Horner's syndrome. X-Ray thickened nasopharyngeal wall. Invasion sphenoid sinus. Erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 9 months later alive and symptom free but still same cranial nerve lesions.

Case 59. Chinese Cantonese Male age 38.

History 3 months epistaxis and nasal obstruction. One month bilateral swellings of neck, temporal headache and deafness. O.E. Bilateral small cervical glands. Small ulcer near right Eustachian orifice. Lesion right XI. Erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 4 months later right ptosis and tinnitus. Did not return. Progress unknown.

Case 60. Chinese Cantonese Male age 50.

History 3 months numb right cheek. One month blurred vision. O.E. Palatal paresis. Bilateral moderate cervical adenopathy. Lesion right XI. Nasopharynx: ulcer of lateral wall. Histology: squamous epithelioma. Lesions right VI, V (1 & 2) X. Treated X-Rays. Failed to complete. Progress unknown.

Case 61. Chinese Hokien Male age 12.

Four months swelling right neck.. One month

temporal headache. 3 weeks swelling left neck.

O.E. Moderate bilateral cervical adenopathy. Ulcer of lateral nasopharyngeal wall. Opacity floor of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Failed to complete radiotherapy. Progress unknown.

Case 62. Chinese Teochew Female age 41.

History 14 months swelling left neck. 7 months swelling right neck, left tinnitus, right deafness. 5 months generalised headache. 4 months epistaxis. 2 weeks diplopia, dysphagia and blurred vision. O.E. Emaciated. Bilateral moderate cervical adenopathy. Rough patch on posterior nasopharyngeal wall. Palatal paresis. Lesions right X and XI. Histology: squamous epithelioma. Treated radiotherapy. Response only slight. Deteriorated. Glands enlarged. 2 months later spastic gait. Retention of urine. Paraplegic. Metastases D5 and D6. Cervical and lumbar spine. Died 18 months from onset. Post mortem reported.

Case 63. Chinese Teochew Female age 49.

History 27 months right cervical swelling. 2 years bitemporal headache. One year left cervical swelling, epistaxis, nasal obstruction. 4 months deafness. 2 weeks blurred vision, diplopia and



dysphagia. O.E. Large bilateral cervical glands. Nasopharynx: huge fleshy mass arising from posterior wall. Palatal paresis. Lesions of right VI, XI, XII and left V (1st and 2nd divisions). X-Ray erosion of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 2 months later dyspnoeic. Ankle oedema. Metastasis in D6 (osteosclerotic) and ribs. Failed to return. Presumed dead.

Case 64. Chinese Hainanese Female age 47.

History 14 months swelling right neck, 13 months left neck. 11 months epistaxis and nasal obstruction. Seven months headache. 5 months tinnitus, 4 months pain in ear. 3 months deafness. 3 months blurred vision and diplopia. 2 months dysphagia. O.E. Emaciated. Moderate bilateral cervical adenopathy. Trismus. Palatal paresis. Nasopharynx: large fleshy growth of left lateral wall. Lesions of left III, VI, V, X, XI, XII and Horner's syndrome. Massive erosion of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. Cranial nerve lesions unchanged. Alive 22 months from onset.

Case 65. Chinese Hokien Female age 57.

History one year epistaxis. 7 months swelling

right neck, 2 months swelling left neck. 7 months occipital headache. 6 weeks blurred vision. O.E. Bilateral moderate cervical adenopathy. Palatal paresis. Lesions of left III, VI, V (ophthalmic) XI and Horner's syndrome. Massive erosion floor of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 7 months later glands recurred. Hoarse. One month later blind. Deteriorating but alive 20 months from onset.

Case 66. Chinese Teochew Female age 14.

History 15 months epistaxis. 8 months swelling right neck. 3 months nasal obstruction and pain in ear. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: small ulcer right lateral wall. Histology: squamous epithelioma. Treated X-Rays. Good response. 8 months later lesion of V (maxillary). Retreated. V lesion recovered. Alive and well 25 months from onset.

Case 67. Chinese Cantonese Male age 36.

History one month epistaxis, followed by nasal obstruction. One month temporal headache. O.E. Palatal paresis. Small nodule in right Fossa of Rosenmüller. Erosion petrous apex. Histology: squamous epithelioma. Treated X-Rays. Failed to complete treatment. Progress unknown.

Case 68. Chinese Cantonese Female age 40.

History 9 months numbness left cheek. 2 months diplopia, squint and temporal headache. O.E. Small raised plaque rear left Eustachian orifice. Lesions of left V (1 & 2) VI and XII. Erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 4 months later lumbar and iliac crest pain. Palpable cervical glands. Progress unknown.

Case 69. Chinese Cantonese Male age 58.

History one year nasal obstruction. Swellings right neck 11 months, left neck 9 months. Deaf 6 months. 11 months felt 'lump in throat'. 4 months headache. O.E. Moderate bilateral cervical adenopathy. Large fungating tumour of right nasopharyngeal wall. Palatal paresis. X-Ray thickening of nasopharyngeal wall. Histology: lymphoepithelioma. Treated X-Rays. Primary responded. Glands unchanged. 6 months later bilateral deafness and cervical glands bigger. Died 21 months from onset.

Case 70. Chinese Cantonese Female age 48.

History 12 months epistaxis. 4 months temporal headache, bilateral tinnitus, dysphagia, hoarseness, cough. O.E. Bilateral palatal paresis. Nasopharynx: huge tumour filling whole of right side. Vocal cord



palsy on right. Gross erosion middle cranial fossa. Histology: transitional cell carcinoma. Treated X-Rays. Failed to complete therapy. Progress unknown.

Case 71. Chinese Hokien Male age 48.

History 12 months pain side of head and face. 8 months epistaxis. 5 months aural discharge. 2 months swelling left neck. O.E. Small left cervical adenopathy. Palatal paresis. Nasopharynx: huge fleshy growth from left lateral wall. Tympanic membrane opaque. Perforated. Serous discharge. Lesions of VI (bilateral) and of left V (all divisions) X and XI. X-Ray. Soft tissue mass nasopharynx. Erosion petrous apex. Histology: squamous epithelioma. Treated X-Rays. Failed to complete therapy. Progress unknown.

Case 72. Chinese Cantonese Female age 27.

History 20 months swelling left neck. One month epistaxis. O.E. 6 months pregnant. Bilateral cervical adenopathy. Palatal paresis. Nasopharynx: fleshy growth arising from left side of posterior wall. Lesions of left V (motor) XI. X-Ray erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive 29 months after onset but with probable spinal metastases.

Case 73. Chinese Teochew Male age 49.

History 3 months epistaxis, nasal obstruction, deafness and tinnitus on right. Parietal headache. Two weeks dysphagia. O.E. Trismus. Nasopharynx: small nodule right lateral wall. Small supra-clavicular gland. X-Ray invasion of sphenoid sinus and erosion body of sphenoid. Histology: anaplastic carcinoma. Treated X-Rays. Good response. 4 months later neuralgia both cheeks. Alive 13 months from onset.

Case 74. Chinese Hokien Male age 44.

History 12 months bilateral swellings in neck. 11 months epistaxis. 4 months deaf, and 'tingling' of face. 5 days dysphagia. O.E. Emaciated. Trismus. Palatal paresis. Nasopharynx: hard nodular growth of right lateral wall. Bilateral large cervical glands. Lesions of left VI, V (motor) and XI, right III, X and XII. X-Ray: swelling in nasopharynx. Round mass at base of skull. Erosion mid cranial fossa. Histology: anaplastic carcinoma. Treated X-Rays. Good response. One month later felt lump in mouth. Blurred vision. Bilateral tinnitus. Trismus so severe could not examine nasopharynx. 2 months later liver enlarged rapidly to umbilicus, nodular. Did not return. Presumed dead.

Case 75. Chinese Teochew Male age 51.

History 6 months epistaxis, nasal obstruction, deafness and tinnitus. 5 months swelling left neck. 4 months generalised headache. O.E. Bilateral small cervical glands. Nasopharynx: fleshy nodular tumour of right Fossa of Rosenmüller. X-Ray soft tissue swelling of nasopharynx. Opacity sphenoid sinus. Erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive and well 18 months from onset.

Case 76. Chinese Cantonese Male age 44.

History 24 months epistaxis, nasal obstruction followed by deafness and tinnitus. 6 months blurred vision. O.E. One small gland below and behind right angle of jaw. X-Ray massive erosion at petrous apex. Tumour encroaching on sphenoid. Histology: squamous epithelioma. Treated X-Rays. Good response. Progress unknown.

Case 77. Chinese Cantonese Male age 24.

History 11 months swelling right neck. 7 months swelling left neck and epistaxis. 3 months nasal obstruction and bitemporal headache. O.E. Palatal paresis. Nasopharynx: pink fleshy tumour of posterior wall on left. Bilateral moderate cervical adenopathy. X-Ray thickening nasopharyngeal wall.



Opacity sphenoid sinus. Histology: anaplastic carcinoma. Treated X-Rays. Good response. Alive 23 months from onset.

Case 78. Chinese Teochew Male age 54.

History 10 weeks swelling left neck. 6 weeks temporal headache. One month swelling right neck. One week shooting pain in side of head. O.E. Bilateral small cervical lymph nodes. Nasopharynx: small raised ulcerated nodule of posterior wall on left. X-Ray. Sclerosis left middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. Progress unknown.

Case 79. Chinese Cantonese Male age 45.

History 3 years swelling right neck. One year swellings in chest. 3 months tightness in chest. 2 months epistaxis, hoarseness and dysphagia. One month blurred vision. 2 months left neck swelling. O.E. Bilateral moderate cervical adenopathy. Vocal cord paralysis on right. Lesions of right X, XI, XII. Two masses in chest overlying and fixed to left seventh rib. X-Ray. Metastases in ribs. Histology: squamous epithelioma. Treated X-Rays to metastases. Fair response. 10 months later further metastases in ribs, scapula and ilium. Presumed dead.

Case 80. Chinese Hainanese Male age 31.

History 10 months tinnitus and deafness. 8 months bilateral swellings in neck. One month epistaxis and nasal obstruction. O.E. Palatal paresis. Bilateral small cervical glands. Tympanic membrane opaque with retraction of drum head. X-Ray erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. 3 months later glands recurred. Deteriorated steadily. 4 months later liver enlarged. Extensor plantar response. Presumed dead.

Case 81. Chinese Hokien Male age 44.

History 3 months swelling left neck. One month right neck and bilateral deafness. O.E. Bilateral cervical adenopathy larger on left. Small elevation near left Eustachian tube. Tympanic membrane opaque. X-Ray erosion middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Responded. Alive and well 11 months from onset.

Case 82. Malay Male age 52.

History 2 months swelling left neck, followed by deafness and tinnitus. O.E. Bilateral small cervical glands. Palatal paresis. Small ulcer of vault above left choana. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive and well 10

months from onset.

Case 83. Chinese Hokien Male age 46.

History 12 months nasal obstruction. 4 months swelling left neck and temporal headache. O.E. Moderate bilateral cervical adenopathy. Palatal paresis. Nasopharynx: large pink fleshy growth of left lateral wall. Lesions left III, V (mandibular and motor) XI. X-Ray thickening nasopharyngeal wall. Erosion floor of middle fossa. Histology: squamous epithelioma. Treated X-Rays. Good response. V lesion went. 4 months later tinnitus. Alive but deteriorating 18 months from onset.

Case 84. Chinese Teochew Male age 53.

History 12 months deafness and tinnitus. 5 months blurred vision. 2 weeks epistaxis, nasal obstruction and bilateral ptosis. One week bifrontal headache. O.E. Palatal paresis. Nasopharynx: fungating tumour of roof protruding down right nostril. Bilateral III, IV and VI lesions, right X and XI. X-Ray thickening posterior nasopharyngeal wall. Tumour in nose. Erosion sella turcica. Histology: transitional cell carcinoma, and tuberculous adenitis. Treated X-Rays. Good response. Ptosis improved on left. Alive 19 months from onset.



Case 85. Chinese Hainanese Male age 44.

History 9 months swelling left neck. 8 months blurred vision, diplopia and epistaxis. 7 months nasal obstruction. Deafness and tinnitus. 2 weeks pain 1st division of V. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: fleshy nodular growth of left lateral wall. Lesions of left II, III, V (ophthalmic) VI, XI. X-Ray gross erosion both middle fossae. Histology: transitional cell carcinoma. Treated X-Rays. Good response. VI lesion went. 4 months later pain left cheek. Retreated. Alive 16 months from onset.

Case 86. Chinese Cantonese Male age 54.

History 6 months nasal obstruction and epistaxis. Four months bitemporal headache. 2 months swelling left neck. O.E. Bilateral small cervical glands. Nasopharynx: fungating tumour of roof protruding down left nostril. Lesions left III, V (motor) and VI. X-Ray thickening nasopharyngeal wall, erosion of middle cranial fossa. Histology: squamous epithelioma. Treated X-Rays. Did not complete course. Progress unknown.

Case 87. Chinese Teochew Male age 46.

History 10 months swelling left neck. 6 months swelling right neck. 4 months epistaxis and nasal

obstruction, deafness. O.E. Bilateral small cervical glands. Nasopharynx: small ulcer of lateral wall. Histology: squamous epithelioma. Treated X-Rays. Good response. Returned 9 months later with multiple secondaries. Progress unknown. Presumed dead.

Case 88. Chinese Teochew Female age 42.

History swelling left neck 11 months, right neck 10 months. O.E. Moderate bilateral cervical adenopathy. Positive biopsy from nasopharynx. Histology: anaplastic carcinoma. Treated X-Rays. Good response. Alive and well 14 months from onset.

Case 89. Chinese Teochew Male age 51.

History swelling of left neck 8 months, right neck 5 months. O.E. Moderate bilateral cervical adenopathy. Palatal paresis. Nasopharynx: ulcer left lateral wall. Histology: anaplastic carcinoma. Treated X-Rays. Good response. Alive and well 17 months from onset.

Case 90. Chinese Hakka Male age 29.

History 2 months bilateral swellings in neck. O.E. Bilateral small cervical glands. X-Ray thickening posterior nasopharyngeal wall. Histology: lympho-epithelioma. Treated X-Rays. Good response. 11 months later glands recurred. Retreated. Poor response. Enlarged. Urethane. Glands slightly

diminished. Recurred one month. Alive 14 months from onset.

Case 91. Chinese Hakka Male age 46.

History 7 months swelling left neck. 5 months swelling right neck. 4 months epistaxis. 3 months tinnitus. 3 weeks occipital headache. 2 weeks dysphagia. O.E. Bilateral large cervical glands. Nasopharynx: hard white nodular growth left lateral wall. Histology: squamous epithelioma. Treated X-Rays. Response good. Died 3 months later, 10 months from onset.

Case 92. Chinese Hokien Female age 69.

History 6 weeks frontal headache. One month bilateral neck swellings, epistaxis, deafness, tinnitus, blurred vision. One week dysphagia. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: fleshy fungating growth of right lateral wall. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive and well  $6\frac{1}{2}$  months from onset.

Case 93. Chinese Cantonese Male age 33.

History 18 months swelling left neck. 13 months temporal headache. One month tinnitus and deafness. O.E. Large left cervical glands. Trismus. Palatal paresis. Nasopharynx: fungating tumour of vault.



Tympanic membrane opaque. Drum head retracted.  
Enlarged axillary glands. Wasting left sternomastoid  
and trapezius. Histology: lymphoepithelioma.  
Treated X-Rays. Good response. One month later  
blurred vision. Alive 24 months from onset.

Case 94. Chinese Hokien Male age 38.

History 10 months temporal headache. 9 months  
swelling right neck and epistaxis. O.E. Moderate  
bilateral cervical adenopathy. Nasopharynx: fleshy  
fungating tumour of right lateral wall. Histology:  
squamous epithelioma. Treated X-Rays. Response  
good. Progress unknown.

Case 95. Chinese Cantonese Male age 57.

History 4 months occipital headache followed by  
epistaxis. 10 weeks left tinnitus, deafness and  
neuralgia cheek. O.E. Palatal paresis. Nasopharynx:  
small nodule left lateral wall. Lesions left V (2nd  
and 3rd divisions) X. Erosion middle cranial fossa.  
Histology: differentiated squamous epithelioma.  
Treated X-Rays. Response slight. 2 weeks later  
lesion left VII. 2 months later hole in hard palate.  
Food regurgitating into nasopharynx. Died 8 months  
from onset.

Case 96. Chinese Hakka Male age 46.

History 2 years bilateral swellings in neck.

Three months deafness and tinnitus. 2 months temporal headache and blurred vision. One month epistaxis. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: white nodular growth on left of posterior wall. Tympanic membrane opaque. Drum head retracted. Lesion left V motor. Histology: lymphoepithelioma. Treated X-Rays. Failed to complete therapy. Progress unknown.

Case 97. Chinese Hainanese Male age 37.

History 2 years pain side of head and face. 21 months bilateral epistaxis and nasal obstruction. 12 months deaf, tinnitus and aural discharge. O.E. Palatal paresis. Nasopharynx: extensive fungating growth of vault. Ear drum perforated. Serous discharge. Exostosis. Lesions left V (motor) VII. X-Ray soft tissue swelling nasopharynx. Erosion petrous apex on left. Histology: squamous epithelioma. Treated X-Rays. Response good. Cranial nerves unchanged. Alive and symptom free 26 months from onset.

Case 98. Chinese Cantonese Male age 43.

History 3 months numbness right cheek. One month deafness, tinnitus, blurred vision. 2 weeks intense itching and watering right eye. 3 days temporal headache. O.E. Nasopharynx: small white

nodule on right of posterior wall. Lesion of right V all divisions. X-Ray erosion petrous apex.

Histology: squamous epithelioma. Treated X-Rays. Good response. Anaesthesia went but had pain right maxillary. Alive 6 months from onset.

Case 99. Eurasian Male age 56.

History 7 months pain in chin. Mandibular avulsion performed, pain recurred 3 months ago. 3 months right deafness and tinnitus. One month nasal obstruction, temporal headache. Swelling right neck. One week epistaxis. O.E. Moderate bilateral cervical adenopathy. Palatal paresis. Nasopharynx: purplish polypoid mass right lateral wall. Tympanic membrane opaque. Drum head retracted. Lesions V both motor, right mandibular nerves. Histology: squamous epithelioma. Treated X-Rays. Good response. Progress unknown.

Case 100. Chinese Cantonese Female age 34.

History 3 years epistaxis. 20 months bilateral deafness and tinnitus, nasal obstruction and bitemporal headache. 4 months squint. O.E. Small left cervical glands. Palatal paresis. Nasopharynx: large fungating mass right lateral wall. Lesions right VI and XI. Histology: squamous epithelioma. Treated X-Rays. VI lesion unchanged. Response



otherwise good. Alive 39 months from onset.

Case 101. Malay Male age 54.

History 4 months swelling right neck, bilateral temporal headache, right tinnitus. One month numb. and pain 1st division V. O.E. Bilateral moderate cervical adenopathy. Nasopharynx: fleshy growth of right lateral wall. Histology: lymphoepithelioma. Treated X-Rays. Refused to complete therapy. Alive 7 months from onset.

Case 102. Chinese Teochew Male age 48.

History one year swelling right neck. Blurred vision. 2 months temporal headache. One month deaf. O.E. Bilateral cervical adenopathy, gross on right, small on left. Nasopharynx: ulcer of right lateral wall. Right vocal cord paralysis. Lesions right X and XI. X-Ray erosion middle cranial fossa. Metastases in vault of skull. Histology: transitional cell carcinoma. Treated X-Rays. Good response. Alive and well 14 months from onset.

Case 103. Chinese Hokien Male age 26.

History 2 months swelling left neck, 6 weeks right. O.E. Moderate bilateral cervical adenopathy. Palatal paresis. Nasopharynx: pink fleshy growth of lateral wall occupying whole left side. X-Ray thickening nasopharyngeal wall. Erosion petrous apex.

Histology: squamous epithelioma. Treated X-Rays.  
Response poor. Alive 5 months from onset.

Case 104. Chinese Teochew Male age 20.

History deaf one year. 4 months epistaxis and nasal obstruction. 3 months swelling left neck. O.E. Small left cervical gland. Irregular hard plaque above Eustachian tube on left. Histology: anaplastic carcinoma. Treated X-Rays. Response good. Alive 15 months from onset.

Case 105. Chinese Hokien Male age 19.

History 3 months epistaxis and nasal obstruction, deafness, tinnitus, swelling left neck. Pain in left cheek and occipital headache. O.E. Small cervical gland. Polypoid tumour from left Fossa of Rosenmüller. Histology: lymphoepithelioma. Treated X-Rays. Response good. Alive 6 months from onset.

Case 106. Chinese Hokien Male age 69.

History 6 months epistaxis. 5 months swelling left neck. 4 months parietal headache. O.E. Bilateral small cervical glands. Nasopharynx: swelling on left of posterior wall. Lesion left V (motor). Histology: squamous epithelioma. Failed to return for treatment. Progress unknown.

Case 107. Malay Male age 50.

History 8 months swelling left neck. One month deafness and tinnitus. O.E. Bilateral cervical adenopathy, gross on left, small on right. Nasopharynx: fleshy growth of left lateral wall.

Histology: squamous epithelioma. Treated X-Rays. Still on treatment.

Case 108. Chinese Hainanese Male age 48.

History one year sore throat. Tinnitus, deafness and aural discharge on right. 8 months swelling right neck. O.E. Bilateral moderate cervical adenopathy. Nasopharynx: large nodular growth on right of posterior wall. Histology: squamous epithelioma. Treated X-Rays. Did not complete course. Progress unknown.

Case 109. Chinese Hainanese Female age 19.

History one year bilateral swellings in neck, nasal obstruction. 7 months parietal headache. 4 months pain and swelling left shoulder. 3 months epistaxis. O.E. Bilateral cervical adenopathy, gross on left extending to shoulder. Nasopharynx: huge fungating growth of left lateral wall. Large soft tumour, cystic in parts, exquisitely tender, left shoulder. X-Ray massive tumour involving shoulder and destroying acromioclavicular joint, eroding clavicle,



acromium and humerus. Histology: squamous epithelioma. Treated X-Rays. Dramatic response. Masses in neck and shoulder disappeared. Alive 14 months from onset.

Case 110. Chinese Hokien Female age 23.

History 14 months swelling left neck, 12 months on right. 7 months epistaxis and nasal obstruction. Six months tinnitus. 5 months blurred vision. 3 months fronto-temporal headache. O.E. Gross bilateral cervical adenopathy. Nasopharynx: fungating growth of posterior wall. Trismus. X-Ray soft tissue shadow nasopharynx. Histology: squamous epithelioma. Treated X-Rays. Good response. Alive 15 months from onset.

Case 111. Chinese Cantonese Male age 37.

History 6 months swelling left neck. 5 months nasal obstruction and temporal headache. 2 months hoarseness. 3 weeks dysphagia. 2 weeks cough and 'choking' feeling. O.E. Moderate bilateral cervical adenopathy. Nasopharynx: fungating tumour on left of posterior wall. Left vocal cord paresis. Lesions left X, XI, XII and Horner's syndrome. Histology: anaplastic carcinoma. Treated X-Rays. On treatment.

Case 112. Chinese Hokien Male age 23.

History swellings left neck 6 months, right neck

five months. 6 months epistaxis, occipital headache and pain left cheek. 2 months nasal obstruction.

O.E. Moderate bilateral cervical adenopathy. Small ulcer above left Eustachian tube. Lesion left V (maxillary). Erosion middle cranial fossa.

Histology: squamous epithelioma. Treated X-Rays.

On treatment.